EXHIBIT 1

Methodological Assessment of Hussain et al. 2021.[1]
Expert Report of Thomas A. Trikalinos, M.D., Ph.D

I. QUALIFICATIONS

I am a Professor of Health Services, Policy & Practice and Biostatistics and Director of the Center for Evidence Synthesis in Health at the Brown University School of Public Health in Providence, Rhode Island. At Brown, I am also the Director of the Brown Evidence-based Practice Center, one of nine such centers in North America designated by the Department of Health and Human Service's Agency for Healthcare Research and Quality (AHRQ) to perform systematic review- and meta-analysis-based assessments of medical technologies. I earned my M.D. and Ph.D. in Epidemiology from the University of Ioannina in Greece. Before being appointed to the faculty at Brown, I held academic appointments at Tufts University and its Institute for Clinical Research and Health Policy Studies in the areas of medicine and clinical and translational science. I have also been a visiting Associate Professor in Computer Science at Tufts University and a visiting Scholar at the Center for Operations Research at the Sloan School of Business of the Massachusetts Institute of Technology.

In addition to my academic appointment, I hold active memberships in several organizations focused on public health and statistics, including the Society for Medical Decision Making, the American Statistical Association, the Institute for Operations Research and Management Science, and the closed-membership Society for Research Synthesis Methodology. I also serve as an Editorial Advisor for the journal *BMC Medical Research Methodology*, and on the editorial board of *Research Synthesis Methods*, and previously served as the Secretary of the Society for Research Synthesis Methodology.

I have developed and taught graduate-level university courses in basic and advanced meta-analysis, as well as short courses that I have taught at conferences, universities and federal agencies such as the Centers for Disease Control and Prevention and the Food and Drug Administration. I have over 200 publications in the medical, statistical and computer science literatures, which have received over 24,000 citations. Many of my publications are on methods and applications of basic and advanced meta-analysis. I have been invited to speak dozens of times regarding the proper methodologies for conducting medical and pharmaceutical studies and systematic reviews and meta-analyses thereof, including the kind of meta-analyses at issue here. I have developed methodological recommendations on the conduct of basic and advanced meta-analysis of treatments and tests and of decision and economic analyses. *See, e.g.*, Fu R, Gartlehner G, Grant M, Shamliyan T, Sedrakyan A, Wilt TJ, Griffith L, Oremus M, Raina P, Ismaila A, Santaguida P, Lau J, Trikalinos TA. Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol. 2011; 64(11):1187-97, a publication of which I am senior author and which informed AHRQ's methodological recommendations for meta-analysis.

Finally, I have extensive experience in creating software for semi-automating processes of evidence synthesis, including open-source and freely available software for basic and advanced meta-analysis in the health sciences (OpenMeta-Analyst) and in evolutionary biology and ecology (OpenMEE). I was also a consultant in the development of commercial software for meta-analysis, such as version 1 of Comprehensive Meta-Analysis (CMA), which is the software used by the Hussain Study (the authors used version 3). *See, e.g.,* Wallace BC, Schmid CH, Lau J, Trikalinos TA. Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol. 2009 Dec 4; 9:80; and Wallace BC, Lajeunesse MJ, Dietz G, Dahabreh IJ, Trikalinos TA, Schmid CH, Gurevitch J. Open MEE: Intuitive, open-source software for meta-analysis in ecology and evolutionary biology. Methods in Ecology and Evolution. 2017 Aug; 8(8):941-7.

My current CV is attached as **Exhibit A**.

II. QUESTIONS ASKED

I was asked by counsel to review and assess the soundness of the methodology and analysis of the meta-analysis contained in the article titled "Perineural Liposomal Bupivacaine is Not Superior to Nonliposomal Bupivacaine for Peripheral Neural Block Analgesia,"[1] (the "Study" or "Hussain Study"), published in the February 2021 issue of *Anesthesiology*, the journal of the American Society of Anesthesiologists.

III. SUMMARY OF OPINIONS

1. The Study suffers from significant methodological errors, including, but not limited to the following: The authors (1) engage in crude, cross-study pooling of respondents—which destroys randomization and creates non-comparable groups—rather than stratified pooling; (2) purport to compare divergent groups across trials, ignoring substantial clinical and methodological diversity among the trials and introducing confounding effects; (3) omit trial results that are favorable to liposomal bupivacaine; (4) improperly correct for "multiple tests"; (5) apply overly broad confidence intervals, which raises the threshold for acknowledging differences between the treatments under comparison; (6) fail to conduct or report adequate heterogeneity analyses; and (7) deviate from recommendations for reporting data, which reduces transparency and prevents full analysis and replication of their work.

2. These errors may be a function of the authors' inexperience with appropriate meta-analysis. However, certain of the design failings raise questions as to whether some or all of the problems may also be caused, in part, by the authors' intent to reach a predetermined outcome.

[1] Hussain N, Brull R, Sheehy B, et al. Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia. Anesthesiology. 2021; 134(2):147-164.

3. I endeavored to recreate the authors' meta-analysis with respect to their primary outcome (differences in the "Area Under the Curve" ["AUC"] of pain scores between 24 and 72 hours post-operatively), applying many of the same protocols, but correcting for some of their more significant errors. The AUC is explained more fully later on, but it is the author's constructed metric to quantify patients' overall pain experience.

    a. The re-analysis finds a mean difference in AUC between 24 and 72 hours post-operatively of 1.77 cm*days (95% Confidence Interval, 0.71 to 2.86), favoring liposomal bupivacaine over nonliposomal bupivacaine, but with substantial statistical heterogeneity. Thus, the re-analysis finds that pain experience on the AUC metric, between 24 and 72 hours post-operatively, were on average 1.77 points better for patients receiving liposomal bupivacaine versus those who received other local anesthetics.

    b. Heterogeneity analyses suggest that the treatment effect of liposomal bupivacaine versus nonliposomal bupivacaine becomes 0.35 cm*day (95% Credible Interval: 0.02 to 0.61) larger for every 1 cm*day increase in the mean AUC in the controls (nonliposomal bupivacaine).

    c. In the subgroup of trials in which the mean AUC of the control group was at least 8.6 cm*day (the mean value of the seven trials in my analysis), the AUC with liposomal bupivacaine was better by 2.85 cm*day (95% CI, 1.84 to 3.87) than that of nonliposomal bupivacaine. For trials where the mean AUC in the controls was less than 8.6 cm*day, the difference in the AUC was 0.49 cm*day (95% CI, -0.05 to 1.03) in favor of liposomal bupivacaine. This subgrouping appears to explain the between-studies statistical heterogeneity. In other words, when the control group (those not receiving liposomal bupivacaine) had low average pain scores, the benefit of liposomal bupivacaine was not as pronounced, but as the average pain scores increased, the difference with liposomal bupivacaine became greater. This may be because the control groups with lower pain scores either endured less painful surgeries, reducing the need for long acting anesthetic, or because the patients were receiving enough other "rescue" medication (e.g., opioids) to mask differences between liposomal bupivacaine and nonliposomal bupivacaine.

    From my re-analysis, I conclude that there is strong evidence that liposomal bupivacaine is more effective than nonliposomal bupivacaine in terms of the difference in AUC metric. The evidence also suggests that the treatment effect of liposomal bupivacaine is larger in trials with higher pain scores in the controls.

IV. OVERVIEW OF META-ANALYSIS REVIEWS IN MEDICAL RESEARCH

Randomized controlled trials are at the heart of modern medical research: Modern medicine is an empirical discipline. Key tools to generate knowledge about the effects (outcomes) of interventions[2] are well-designed, -conducted, and -analyzed experiments referred to as *randomized controlled trials*. These experiments enroll persons (patients) with a particular condition and then divide them into two or more groups, with each group receiving an intervention. The patients are *randomly assigned* to their groups. Then the researchers follow up with patients and measure and compare patient outcomes.

The term *outcomes* refers to measurements in or experiences of patients with each intervention. Examples of outcomes are the mean pain score at 24 hours post-operatively, or the proportion of patients who are pain free at the same time point. The *intervention effect* is the difference in outcomes between the intervention and its comparator, and it is essentially the *result* of the trial.

The random assignment of patients to interventions ensures that, on average, the patients who receive each intervention *are comparable with respect to observed and unobserved factors* that can affect their outcomes. If the compared groups are balanced for all known and unknown effect modifiers and confounding factors, then differences in the outcomes can only be attributed to the different interventions.

Two important observations follow:

1. Not all randomized trials are well-designed, -conducted, and -analyzed, and methodological expertise is needed to assess potential problems with a specific trial.

2. The patient groups that are compared in randomized trial should “go together” because, in principle, they are as similar as they can be. This is important for how to meta-analyze results from two or more randomized trials, as discussed below.

Impetus for evidence synthesis: Currently, about 700,000 randomized trial reports exist in PubMed, an online repository of mostly peer-reviewed medical research papers, and it is estimated that about 100 trials are published every day. For a particular clinical question, such as the effects of peripheral nerve blocks with liposomal versus nonliposomal bupivacaine on post-operative pain, several randomized trials may exist. These are not carbon-copies of each other: They differ in the types of patients they enroll (e.g., types of surgeries), the exact comparators (e.g., dose for each drug, supplemental pain relief protocols), and outcomes they measure, and so on. However, it is possible that they can all inform the conceptual question of how the interventions compare in general. We often use the term *clinical and methodological diversity* to refer to differences in clinical, epidemiological, design, and other attributes of the

[2] Interventions can include giving a drug, doing a surgery, administering a test, or more-complex patient management strategies, e.g., administering liposomal bupivacaine after surgery with a prespecified protocol for supplemental post-operative analgesia (pain relief) with other drugs on an as-needed-basis.

studies in an evidence synthesis. In practice, some degree of clinical and methodological diversity exists in every evidence synthesis.

It is therefore important to synthesize all practically available evidence on the effects of interventions for the question at hand. This task is called *evidence synthesis*. A typical evidence synthesis involves a *systematic review* of the literature, which is a structured, protocol-driven approach to find all practically identifiable trials that address the question of interest, extract information from them, assess their methodological rigor, and synthesize their results. All systematic reviews should synthesize trial results qualitatively. In many systematic reviews, it is possible to perform *meta-analyses*, which are quantitative syntheses of the results of individual trials.

What is a meta-analysis: A meta-analysis of randomized trials aims to characterize the distribution of the results of a set of trials. Otherwise put, a meta-analysis is a sort of averaging that has two primary goals: First, it can be used to estimate the mean of the studies' results and the degree of difference between study results, among other things. We often use the term *statistical heterogeneity* to refer to the extent of differences in study results. Second, it can be used to explore whether any differences in study results are associated with differences in study characteristics (e.g., pain levels, type of surgery, drug dosage, methodological characteristics); i.e., whether clinical and methodological diversity of study characteristics manifests as statistical heterogeneity in studies' results.

Standards for performing meta-analyses: Because of the importance of evidence synthesis in developing clinical guidance, several national and international bodies have developed recommendations and standards for performing systematic reviews and meta-analyses. These include the AHRQ Evidence-based Practice Centers Methods Guide, the methodological recommendations of the Cochrane Collaboration, and the standards of the former Institute of Medicine of the National Academies of Sciences.[3] All these recommendations are in essential agreement.

The following are generally accepted principles of meta-analysis methodology:

Meta-analysis estimates a *weighted average* of the studies' results so that studies that are more precise receive larger weights compared to studies that are less precise. Specifically, studies receive weights that are between 0 and 1 (equivalently, 0% and 100%) and add up to 1 (or 100%). In other words, each study's weight is the proportional contribution of that study's result to the meta-analysis average. The industry standard is to use weights that are inversely

[3] These guides include, for example (non-exhaustive list): (i) a series of about a dozen papers starting with Slutsky J, Atkins D, Chang S, Sharp BA. AHRQ series paper 1: comparing medical interventions: AHRQ and the effective health-care program. Journal of Clinical Epidemiology. 2010 May 1; 63(5):481-3; (ii) Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions. 2d Edition. Chichester (UK): John Wiley & Sons, 2019; (iii) Morton S, Berg A, Levit L, Eden J, editors. Finding what works in health care: standards for systematic reviews. Institute of Medicine of the National Academies.

proportional to the variance of the result of each study.[4] "Variance" is a technical term: It is a quantification of the statistical uncertainty that accompanies a study result. Using inverse-variance weights results in the statistically most-efficient averaging: The resulting meta-analysis mean will have the smallest variance compared to any other set of weights that are between 0 and 1 and sum to 1. For example, inverse-variance weighting is more efficient than weighting proportionally to study sample size—sample-size weighting is not an industry standard. Using different weights can skew meta-analysis results.

In practice, to do a proper meta-analysis one needs two so-called *sufficient statistics* from each trial: (i) an estimate of the mean intervention effect (e.g., as relevant here, a mean difference in pain scores between liposomal bupivacaine and nonliposomal bupivacaine) and (ii) the trial's variance. Extracting this information from trial reports is sometimes easy (e.g., when it is directly reported), but other times it can be more involved. Of relevance to this report, if one is interested in an outcome that is not directly reported in a trial but is a function ("a composition") of other outcomes that are reported in the trial, the mean and variance of this outcome may have to be estimated using standard, but somewhat advanced, techniques, such as the multivariate delta method. The multivariate delta method is a way to estimate the mean and variance of a "composite" outcome from the reported means and variances of its individual "components" and information on their correlations.

The following are key observations:

1. Patient groups are comparable *within* randomized trials but not *across different trials*. A meta-analysis should find an average for differences *within* each study between the intervention and its comparator in each trial. These within-study differences are obtained by comparing like-with-like patients. In other words a meta-analysis should average the results (intervention effects) of individual trials.

2. It would be wrong to first aggregate outcomes per patient group (per intervention) across all studies and then take the difference of these aggregations. For example, it is wrong to average the pain scores for all patients who received a certain intervention in all studies, then average the pain scores of all patients who received a comparator intervention in all studies, and then take the difference between these aggregations. Such an approach is called "crude pooling" or "naïve pooling." It ignores the fact that groups from the same randomized trial should "go together," breaks randomization and loses all its benefits, and can yield nonsensical results. For example, a meta-analytic average should always fall between the minimum and the maximum results (treatment

[4] This is referred to as inverse-variance weighting. Depending on the specifics of a problem, more-elaborate methods are used that follow the same philosophy and have statistical properties analogous to or better than inverse-variance weighting. Weighting by sample size does not have such statistical properties.

effects) of individual studies. With "crude pooling," one can get answers that are smaller than the minimum or larger than the maximum of study results, which makes no sense.

Finally, while patients are comparable within each randomized trial, they are not necessarily comparable across trials. This means that, while one can always meta-analyze a group of trials, the result may have limited or no clinical interpretation if the clinical and methodological differences between the trials (e.g., different surgeries, different doses, different interventions, etc.) are too great. In practice, whether or not a meta-analysis is meaningful for a particular purpose is a judgment call. The industry standard, however, is to *perform heterogeneity analyses*, which explore the impact of the different clinical and methodological study characteristics on the outcome of a meta-analysis and its conclusions. Examples of heterogeneity analyses are *subgroup analyses*, which compare results in subgroups of studies according to levels of the aforementioned factors, and *meta-regression analyses*, which perform analogous comparisons with a statistical (regression) model, possibly for more than one factor at a time. At a minimum, subgroup analyses are almost always possible.

Reporting of meta-analyses: The standing recommendation for reporting of meta-analysis results is that it should be done in a way that allows the results' replication by a third party. Detailed reporting recommendations exist for different types of meta-analyses. Generally, it is standard to report trial-specific numerical data and results in graphs, tables, or in online repositories such as the Systematic Review Data Repository.[5]

V. THE HUSSAIN STUDY IS REPLETE WITH NUMEROUS METHODOLOGICAL ERRORS THAT SKEW THE OUTCOME OF THE ANALYSIS

A. About the Hussain Study

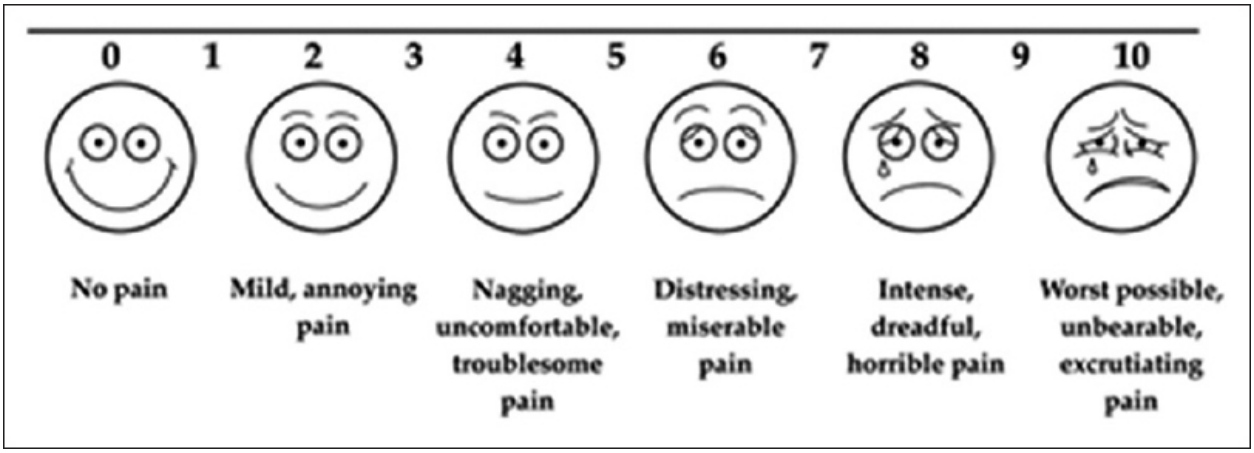
The February 2021 issue of *Anesthesiology* published by the American Society of Anesthesiologists, included a meta-analysis titled "Perineural Liposomal Bupivacaine is Not Superior to Nonliposomal Bupivacaine for Peripheral Neural Block Analgesia" (the "Study" or "Hussain Study"). The meta-analysis was authored by Nasir Hussain, M.D., M.Sc., et al., and it purported to synthesize and evaluate randomized trials that compared liposomal bupivacaine to nonliposomal bupivacaine when used as a peripheral nerve block. Bupivacaine is an analgesic that can be injected directly into tissue to numb a specific area of the body, especially following surgery, or it can be used as a nerve-blocking agent to facilitate post-operative pain management. Liposomal bupivacaine is a modified form that uses a liposomal encapsulation to permit a slow-release of the bupivacaine to the injected site, with the intent of achieving pain relief for a more prolonged period than nonliposomal bupivacaine.

The Hussain Study sought to conduct a meta-analysis of trials that compared a single injection of liposomal bupivacaine (optionally mixed with nonliposomal bupivacaine) to a single injection

[5] Accessible at https://srdrplus.ahrq.gov. This federally funded repository is developed and maintained by the Center for Evidence Synthesis at Brown University, which I direct.

of nonliposomal bupivacaine in adult patients. It sought to assess differences in short-term pain among patients, as well as "long-term outcomes, including persistent postsurgical pain, opioid dependence, and health-related quality of life."[6] The authors identified the randomized trials for review by conducting a published-literature search and queries in registries including www.clinicaltrials.gov. *Id*. From that universe, the authors identified 470 citations. They then culled the list to exclude studies that did not satisfy the Study's eligibility criteria, such as studies that did not use nonliposomal bupivacaine as a comparator, lacked available data, or were not randomized. *Id.* This resulted in a set of nine trials for review. *Id.*

Among other outcomes, the Study purported to compare the overall pain experience between 24 and 72 hours post-surgery of patients treated with liposomal bupivacaine versus those treated with nonliposomal bupivacaine by means of an "Area Under the Curve" ("AUC") metric. More specifically, at any time, a patient's pain can be measured with a Visual Analogue Scale (VAS) between 0 (no pain) to 10 (worst possible pain imaginable). In lay terms, the VAS is a scale that patients may be familiar with in which a healthcare provider asks a patient to rate their pain on a 0-10 scale. It is graphically depicted as follows:



To summarize VAS measurements at 24, 48, and 72 hours post-operation, the authors chose to graph the average VAS scores at these three times and estimate the mean Area Under the [VAS] graph—which is the aforementioned AUC. In lay terms, the AUC aims to quantify an overall pain experience, on the basis of three pain VAS measurements, between 24 and 72 hours post-operatively. As defined, the difference in the AUC should be measured in [VAS units]*[days] or [cm]*[days]—given that a common VAS uses 1 cm per each pain level.[7] As defined in the Study, the AUC with a treatment can take values between 0 cm *day (when pain scores are 0 at 24, 48 and 72 hours post-operatively) and 20 cm*day (when pain scores are 10

[6] In page 2 of Hussain N, Brull R, Sheehy B, et al. Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia. Anesthesiology. 2021; 134(2):147-164 [hereinafter, "Hussain Study"].

[7] The Study mistakenly states that AUC results are reported in cm*hours—all their results for AUC analyses should be scaled by a factor of 24 if that were the case, because there are 24 hours in one day.

for all time points – i.e., for two days). Analogously, the difference in AUCs between two treatments can take values between -20 cm*day and 20 cm*day.

Based on its examination of these nine trials, the Study concluded that liposomal bupivacaine "provides a statistically significant but clinically unimportant improvement" in the AUC score of "postoperative pain scores compared with nonliposomal bupivacaine."[8]

A. The Design and Analysis of the Hussain Study Are Deeply Flawed

As discussed below, it is my opinion that the Hussain Study suffers from serious methodological and statistical failings. These errors, at minimum, suggest inexperience and a lack of familiarity with proper methods, but some evince an intent to reach a predetermined outcome that liposomal bupivacaine does not result in different outcomes from nonliposomal bupivacaine. These errors, when compounded, result in an outcome that is drastically skewed. When a proper meta-analysis is conducted, the resulting outcome is favorable to liposomal bupivacaine.

1. The Hussain Study is Plagued with Multiple Methodological Flaws

The Hussain Study suffers from a number of methodological flaws, at least two of which are particularly significant in how they deviate from established norms and in their potential to skew the outcome of the meta-analysis: The Study employs a method of crude pooling, rather than stratified pooling for the analysis of its primary outcome (the AUC), and it does not explore the substantial clinical and methodological heterogeneity (diversity) of the underlying studies. In addition to those flaws, I identify three others below, which comprise a non-exhaustive list of flaws I observed in my review of the Hussain Study and, when compounded, increase the risk of affecting the outcome of the review.

First, the Study employs flawed "crude pooling" or "naïve pooling" rather than the methodologically correct and recommended "stratified pooling." The correct approach involves two parts: (1) estimate the difference in outcome per study, and (2) synthesize (i.e., average) the study-specific differences. That is, a meta-analysis synthesizes the *results* of the underlying studies, i.e., the differences in AUC that each trial found. Within each randomized trial, these differences in AUC are not subject to systematic errors because the treatments are compared in similar patients.[9] By contrast, the Hussain Study effectively (i) breaks up each trial into treatment and control groups and aggregates VAS scores separately for each timepoint (24, 48, or 72 hours post-op) and treatment (liposomal bupivacaine versus nonliposomal bupivacaine) as if they came from the same study. Then (ii) it calculates a "difference in AUC" based on these aggregations. By indiscriminately merging the treatment and control groups across different sets of trials for different timepoints, the Hussain Study approach creates non-comparable groups. This concept is called "crude pooling," and it is a flawed approach that results in systematic errors and biased results.

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[8] Hussain Study at 11.

[9] For well-designed and -conducted randomized trials.

To illustrate the effect of crude pooling, consider, for example, two hypothetical studies that compare the mortality rate of a blue pill to a red pill. In the first study, there are ten deaths out of 100 patients who receive the blue bill, and 100 deaths out of 1000 patients for the red pill. The death rate for each is 10%, or 0.1. In the second study, there are 50 deaths out of 100 patients who receive the blue pill, compared to five deaths out of ten patients who receive the red pill. Again, the death rate for both is equal, this time at 50%, or 0.5. Both studies find *no difference in the risk of death between the red and blue pills*, and a meta-analysis of these studies *should also find no difference between the two groups.* Using a crude pooling method, the numbers of dead and alive patients are aggregated for each treatment across the two studies, resulting in a total of 60 out of 200 patient deaths with the blue pill (30%, or 0.3), versus 105 out of 1010 patients who receive the red pill (approximately 10%, or 0.1). The crude pooling method suggests that the blue pill caused death 30% of the time, compared to only 10% for the red pill, indicating that the red pill is much safer, which is false. Crude pooling created two non-comparable groups: Almost all patients for the red pill come from the first study, in which patients experience a lower risk of death, but from the blue pill, half of the patients come from the lower risk study. The apparent difference in death rates between the red and blue pills with crude pooling is due to the different composition of the groups and not the differential effects of the pills on mortality.

Fig. 1: Crude vs. Stratified Pooling Illustration

Study	Deaths/Total, blue pill	% deaths, blue pill	Deaths/Total, red pill	% deaths, red pill	Risk difference
1	10/100	0.1	100/1000	0.1	0
2	50/100	0.5	5/10	0.5	0
Crude Pooling	60/200	0.3	105/1010	0.1	0.2

More generally, crude pooling is problematic because it breaks up randomized trials into treatment and control groups that are then merged indiscriminately. This annuls the key advantage of randomized trials, which is that they compare like patients: Randomization, the process of *randomly assigning patients to treatments,* ensures that on average all *known and unknown* confounding factors are balanced between the compared groups so that the only factor that differs is the treatment given to each group. Thus, any differences in outcomes can be ascribed to the difference in treatments.

Crude pooling is a fundamental mistake because it ignores stratification by study and destroys randomization. Methodological recommendations caution against it, and it is routinely used as an example of how *not to do a meta-analysis* during instruction of students and trainees. It is also highly unusual: I cannot remember a publication that used crude pooling for meta-analysis in the last 20 years.

Second, every meta-analysis presents an opportunity to explore whether the clinical and methodological diversity of the synthesized studies explain any differences in study results. This is because studies differ in their *populations* (e.g., types of patients, surgeries, peripheral nerve blocks), *interventions* and *comparators/controls* (e.g., whether patients were given liposomal bupivacaine only or mixed with nonliposomal bupivacaine; what doses were used; whether there were specified protocols for residual-pain management, and what these protocols were), *outcome definitions* (e.g., the exact instruments used for the pain assessment), and *designs* (e.g., what methods were used to guard against common threats to the validity of results including confounding, selection, and measurement biases; extent of missing information, and how missingness was handled). If these clinical and methodological differences are too extensive, the results of a meta-analysis would be meaningless, and the meta-analysis should not be performed. This is why the industry standard is to perform heterogeneity analyses, as discussed above.

In the problem at hand, the included trials are very diverse, but the Study presents no results for heterogeneity analyses. For example, the severity and type of pain a patient experiences varies dramatically across different types of surgeries, and yet the Study puts together patients of vastly different surgeries, including "major shoulder surgery, rotator cuff surgery, arthroscopic shoulder surgery, hip arthroscopy, total knee arthroplasty, video-assisted thoracoscopic surgery, minimally invasive lung resection, inflatable penile prosthesis placement, and total mastectomy," without showing whether and how results change for studies of different indications.[10] The Study also ignores other significant differences, such as in the interventions, including but not limited to administered doses and their timing; types of pre-incisional, surgical, and supplemental post-operative analgesia; and whether liposomal bupivacaine was administered solo or in combination with nonliposomal bupivacaine. A meta-analysis—which, at its core, is an averaging mechanism—is very difficult to interpret when fundamental differences across studies modify or confound the treatment effect.

Third, the Study reports that for mean AUC differences, "[t]he results of individual studies were weighted by their sample size."[11] The industry standard in meta-analysis is to weight study results proportionally to the inverse of their variance, not by sample size or any other metric. This is because inverse-variance synthesis is the most statistically efficient approach—it results in narrower confidence intervals for the meta-analysis mean compared to alternative meta-analysis weighting schemes. The default methods implemented in all widely used pieces of software, including those used by the Study authors, is an inverse-variance synthesis. However, this requires estimating the variance of the difference in AUC in each study, as mentioned earlier.

Fourth, the Study ignores stochastic dependencies between successive measurements of pain levels in the same patients. In other words, the Study looks at reports of pain across all study

[10] Hussain Study at 4.
[11] Hussain Study at 3.

subjects at the 24-hour, 48-hour, and 72-hour post-operative periods *as if they were independent,* without consideration to the fact that patients' pain scores at each interval are likely correlated, and thus the mean VAS scores across timepoints are also likely correlated. For example, if results are positively correlated, a patient who reports a high pain score at the 24 hour mark is likely to also have high scores at 48 and 72 hours. Because between-outcome correlations are not reported by individual trials, the common practice would be to run a sensitivity analysis for various plausible correlations. Failing to account for correlations can change the variances, which can affect the weights in the meta-analysis and confidence intervals of the meta-analysis means.

Fifth, when the standard deviation used in an underlying trial was not available, the Study authors attempt to impute it based on the median standard deviation observed in the other trials.[12] This inherently introduces uncertainty and the risk of error. At minimum, the authors should have imputed a range or distribution of standard deviations and not relied on a single-value imputation. A range or distribution would help account for the fact that standard deviations can differ across trials.

In short, two methodological errors in particular are significant mistakes and carry a material risk of inaccurately skewing the meta-analysis outcome. These failings, when coupled with three other flaws, only compound that risk.

2. Many Choices Made by The Hussain Study Tend to Minimize the Difference Between Liposomal and Non-Liposomal Bupivacaine

If one looks hard enough, one can likely find some inadvertent flaw in even high-quality meta-analyses. However, in addition to the deficiencies identified above, several additional methodological and analytic errors and choices in the Study all would skew in the direction of finding no difference between liposomal and nonliposomal bupivacaine, raising questions of whether the errors were, in fact, inadvertent.

First, the authors omitted results from a trial by Paul Sethi et al., which favors liposomal bupivacaine with an AUC of 3.54 units*days, which indicates a mean improvement on the 0–10 pain scale of 3.54 points between 24 and 72 hours post-operatively. The Study's authors admit that Sethi et al. meets eligibility criteria and claim it was excluded because of a "lack of available data." However, the Sethi trial and its data were reported in a 2019 peer-reviewed publication—well within the Hussain Study's search timeframe.[13] The authors appear to include information from the Xie study (reference 78), which reports VAS scores using a three dimensional plot, making it difficult to accurately extract differences in AUC without special

[12] Hussain Study at 3.

[13] Sethi PM, Brameier DT, Mandava NK, Miller SR. Liposomal bupivacaine reduces opiate consumption after rotator cuff repair in a randomized controlled trial. J Shoulder Elbow Surg. 2019 May; 28(5):819-827.

manipulation of the image to transform it to a typical graph.[14] It is not clear how the Xie data were obtained or extracted.

Second, for their secondary outcomes, the authors made the controversial and counter-to-recommendations choice to *attempt to correct for "multiple tests" in the context of a meta-analysis*. The idea is that when one compares two treatments with respect to many outcomes, one may find differences by chance where no genuine differences exist. This is called a "false positive finding." To minimize the chance of "false positive findings" one can raise the bar for accepting that an observed difference is beyond what would be expected by chance; said another way, one can make more stringent the threshold for determining that two treatments are, in fact, different. One such correction for multiple tests is the Bonferroni–Holm correction, which the Study authors use. Standard meta-analysis guidance, including the methodological recommendations of the Cochrane Collaboration, which the authors report following, states that "[a]djustments for multiple tests are not routinely used in systematic reviews, and we do not recommend their use in general."[15] The reasons for recommending against comparisons for multiple tests are numerous and technical. An important but subtle explanation is that in meta-analysis, we are interested in estimating the magnitude of the mean difference in outcomes between two treatments (a task of *inference*) and not in a yes/no answer of whether the treatments are, in fact, different beyond a chance finding, irrespective of the magnitude of the difference (a task of *testing*). *Inference* and *testing* are distinct technical concepts. In other words, an author would likely use the Bonferroni–Holm correction in a meta-analysis if she was highly inexperienced in conducting such an analysis and unfamiliar with the guidance, or if she desired, from the outset, to reach a determination that there was not a difference between the two analgesics.

Third, the Study opts to describe results of secondary outcomes using a 99% confidence interval, which is broader than a standard 95% confidence interval. One reason to use this wider confidence interval is to try to control for "false positive findings" by making it more difficult to claim that a difference between the treatments is beyond what is expected by chance. This is related to correcting for "multiple comparisons," discussed above. This makes it less likely that the result will demonstrate a difference between liposomal bupivacaine and nonliposomal bupivacaine. However, as mentioned above, the typical and recommended approach in meta-analysis is to forgo efforts to control for "false positive findings" and instead focus on estimating the magnitude of treatment effects using standard 95% confidence intervals.

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[14] Such manipulations involve changing the projection angle of the three-dimensional image and removing the three-dimensional perspective. They require specialized image manipulation software or custom computer code and are pending for my re-analysis. The Hussain Study does not hint at undertaking such a specialized approach to digitize the Xie trial results and does not mention that they received the data from Xie in a personal communication.

[15] Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition. Chichester (UK): John Wiley & Sons, 2019.

Last, the Study does not follow recommended practices for reporting the data and its analyses. This information is not only standard to include but necessary for the results to be reviewed, tested, and replicated. The Study lacks all trial-level numerical information for outcomes, as well as identification for which studies it was necessary to impute missing data. Further, the Study authors state that they contacted the authors of the underlying trials,[16] but it does not describe or reproduce the information, if any, that was obtained in those private communications. Much of this information is typically included in Tables and Figures in the main text, especially for the main outcome analysis, in an appendix, or in online archival tools such as the Systematic Review Data Repository (https://srdrplus.ahrq.gov). This was not done here.

For these reasons, it may be that the Study authors are inexperienced and unfamiliar with an appropriate meta-analysis, which could explain the methodological errors identified above. However, these additional design problems raise questions about whether the problems with the Study arise solely from inexperience or may also be driven by an intent to reach a predetermined outcome.

3. Additional Errors Further Undermine Confidence in the Authors' Familiarity with a Proper Meta-Analysis

In addition to the failings noted above, several additional errors, although minor in comparison, cast doubt on the authors' proficiency in statistical analysis and proper meta-analysis.

First, the Study mistakenly refers to the AUC as the "receiver operating characteristics curve,"[17] but a "receiver operating characteristic curve" (ROC) is something different from their "Area Under the Curve" (AUC). ROCs concern only studies of diagnostic tests, which this is not.

Second, the Study refers to a "Mantel–Haenszel *random*-effects *model*,"[18] but no such thing exists. Mantel–Haenszel is a *method*, not a model, and it concerns *fixed* or *equal* effects, not random effects. A "model" is a specific technical term—a mathematical construct that describes how data are generated, which is distinct from a "method," which is a procedure that does not make assumptions about how data are generated.

Third, the Study contains nonsensical statements and claims. A layered example follows: The underlying studies reported data in two forms, namely *continuous outcomes* (e.g., a study that reports a *mean* pain score) and *binary* or *categorical outcomes* (e.g., the proportion of patients who are pain-free). A simple way to meta-analyze pain score information reported as continuous and binary in different studies is to (1) approximately transform, invoking assumptions that rarely hold, the binary outcome metrics (e.g., the "log odds ratio") to continuous metrics (*standardized mean differences*), and (2) meta-analyze the continuous

[16] Hussain Study at 3.
[17] Hussain Study at 1.
[18] Hussain Study at 3.

metrics across studies.[19] However, the Hussain Study states that it used "the log (odds ratio)" for certain trials that reported *continuous* data.[20] This is meaningless because a log odds ratio is defined only for binary and not for continuous data. Similarly, the Hussain Study also claims to have transformed the log odds ratios to standardized mean differences when studies reported "continuous data," *id.*, which also does not make sense.

Fourth, the Study inconsistently describes its methodologies. For example, it states that it applied an inverse-variance meta-analysis for all continuous outcomes, but it did not do so with regard to the differences in AUC, which is a continuous outcome (the Study refers to weighting by sample size for analyses pertinent to the AUC outcome).[21] As another example, the authors claim to perform random-effects meta-analyses for all outcomes, even though, again, for the AUC they use sample-size weights.

Fifth, the Study misapplies and mischaracterizes the Egger test, a procedure that examines for the presence of systematic differences between more-precise studies and less-precise studies. Even though the Egger test is intended to find so-called "small-study effects" (which can arise due to treatment effect heterogeneity; differences in choices for power analyses in the individual studies; publication, selective reporting and other biases; or chance), the Study mischaracterizes it as a test for "publication bias" (the risk that a study is more likely to be published depending on its findings), when publication bias is only one of numerous situations that can result in a signal with the Egger test.[22] Interpreting the Egger test results as only identifying publication bias can be considered a marker of superficial familiarity with the methodology. Further, the Study apparently misapplies the Egger test because it applies it whenever there were at least three studies available for an outcome. However, simulation analyses suggest that many more studies (at least 10 and possibly over 20 based on various methods studies) are needed for the test to work properly.

Finally, the authors appear to conflate the concepts of *Conflict Of Interest (COI)* and *[Risk of] Bias*: The authors declare that "[i]ndustry-sponsored trials were *a priori* considered a potential source of bias,"[23] and single out and emphasize the result of a sensitivity analysis that excludes an industry-funded trial. There is no empirical justification for assuming that industry-sponsored studies have a high risk of bias, as discussed in the Cochrane Handbook that the

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[19] More elaborate, and perhaps better, methods exist, including a multivariate meta-analysis of binary and continuous outcomes, but to the best of my knowledge, they are not included in the pieces of software cited by the Study and require substantial technical expertise.

[20] Hussain Study at 3.

[21] Hussain Study at 3.

[22] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997 Sep 13; 315(7109):629-34. doi: 10.1136/bmj.315.7109.629.

[23] Hussain Study at 5 (excluding Vandepitte C, Kuroda M, Witvrouw R, Anne L, Bellemans J, Corten K, Vanelderen P, Mesotten D, Leunen I, Heylen M, Van Boxstael S, Golebiewski M, Van de Velde M, Knezevic NN, Hadzic A: Addition of liposome bupivacaine to bupivacaine HCl versus bupivacaine HCl alone for interscalene brachial plexus block in patients having major shoulder surgery. Reg Anesth Pain Med 2017; 42:334–41).

authors purport to follow.[24] Such an assumption would conflate the concept of *Conflict Of Interest (COI)* with the concept of the *[Risk of] Bias*:

1) COI means that there is a suspected or definite incentive for favoring one conclusion over the other, *irrespective of whether the research is biased or not*. The Institute of Medicine describes *financial COI*, e.g., for specialists who perform a profitable procedure, or the manufacturer of a technology, and a range of *non-financial COI*, e.g., for researchers who have taken strong public positions on a topic, or journal editors who wish to publish results that challenge current practice or beliefs and spur scientific discussion. The COI may be associated with money, fame, or a zeal to support a belief. This is why the emphasis is on managing COI to minimize the likelihood that it results in a bias. It is good practice to do sensitivity analyses by subgrouping studies according to whether they have COI or not.

2) By contrast, bias refers to systematic error, meaning that *the result that the study found differs from what it would have found if it was designed, conducted, and analyzed in a correct (unbiased) fashion*. Because it is often impossible to know for sure whether a study result is biased, we usually assess a study's *Risk of Bias*. Assessing the Risk of Bias is a challenging and time-consuming exercise. It is recommended to be done with the aid of structured tools, such as the Cochrane Risk of Bias tool. These tools help systematic reviewers structure their assessments about whether a particular study result is at low, moderate, or high risk of bias.

The Cochrane Risk of Bias tool, which the authors use, and similar tools by the Evidence-based Practice Centers Program of AHRQ *do not automatically consider industry sponsorship an indication of a high risk of bias*. There is wide agreement among methodologists on this note (see for example the editorial by Cochrane methodologist Jonathan Sterne "Why the Cochrane risk of bias tool should not include funding source as a standard item"[25]). Briefly, some empirical data suggest that there are differences in the magnitude of findings between industry-sponsored and non-industry sponsored trials,[26] but, per the Cochrane Manual, at the same time, (i) the industry-sponsored trials tend to be better designed and reported[27] and (ii) they may be done in selected populations or settings or versus inactive comparators. Studies performed in selected populations and settings or versus inactive comparators *are not biased*—

[24] Boutron I, Page MJ, Higgins JPT, Altman DG, Lundh A, Hróbjartsson A. Chapter 7: Considering bias and conflicts of interest among the included studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021

[25] Sterne JAC. Why the Cochrane risk of bias tool should not include funding source as a standard item. Cochrane Database of Systematic Reviews 2013; 12: ED000076.

[26] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L: Industry sponsorship and research outcome: Systematic review with meta-analysis. Intensive Care Med 2018; 44:1603–12.

[27] For example, they are more likely to blind participants or researchers to which treatment was received.

whether or not to include them in a meta-analysis depends on the eligibility criteria of the meta-analysis and the questions it asks.

B. The Culmination of Errors in the Hussain Study Skewed the Results—a Proper Meta-Analysis Results in a Positive Outcome for Liposomal Bupivacaine

As explained above, due to clinical and methodological diversity of the underlying trials, the trials do not lend themselves to meta-analysis. However, because the Hussain Study attempts to conduct a meta-analysis, but its efforts are deeply flawed, I endeavored to recreate the meta-analysis using the correct meta-analytical methods. For the results listed in this section:

1. I did not conduct my own literature searches and citation screening. I retrieved only trial reports for the trials identified by the Study authors.

2. Because the Study did not report study-specific numbers for the difference in AUC, I extracted the pertinent information from the original sources.

    a. I used the same approaches described by the Study authors for imputing missing means and standard deviations from other statistics (medians, interquartile ranges). However, I have not yet performed any sensitivity analysis for the imputed missing statistics.

    b. When needed, I extracted data from plots using a digitizing software.

3. I used the multivariate delta method to estimate the mean difference in AUC and its variance within each trial, so as to do an appropriate meta-analysis. For the meta-analysis, I fit a random-effects model with restricted maximum likelihood.[28]

4. Following the protocol of the Hussain Study, I excluded trials that did not report VAS scores at all three time points. These were Weksler et al., who did not report results for pain at 72 h, and Khandhar et al., who did not report results for pain at 24, 48, or 72 hours. Thus, unless the Hussain Study authors have received the missing data through private communications, they should, per their protocol, have also excluded Weksler and Khandhar from the AUC analyses. Thus, I believe that I analyzed the same underlying articles as the Hussain Study, with, perhaps, two exceptions:

    a. I added data from the Sethi et al. trial, which was deemed eligible by the Hussain Study. However, the Hussain Study did not find the paper that presented the data.

[28] For the purposes of this description, the approach I used weights trial results proportionally to the inverse of the variances. Fitting a random effects model with restricted maximum likelihood is a recommended approach for meta-analyses like the one at hand.

b. I did not include results from the Xie et al. report because it does not provide readily extractable data. The pertinent mean pain VAS data are given in a three-dimensional graph, which requires specialized image manipulation to extract them correctly. I have not yet performed this image manipulation.

5. I did only basic heterogeneity and sensitivity analyses. Further such analyses may yield additional insights. I performed:

   a. A standard heterogeneity analysis that examines whether the magnitude of the difference in the AUC depends on the average level of pain experienced by the patients in a trial. This is a "control-response meta-regression" analysis. The idea is that the level of pain in the controls captures information about how painful the particular operation is, the patients' pain tolerances, and how much the supplemental post-operative analgesia alleviated patients' pain. This analysis can help detect whether the effect of liposomal bupivacaine vs. nonliposomal bupivacaine is bigger or smaller in patients experiencing different levels of pain.

   b. A standard leave-one-out sensitivity analysis and an analysis that assumes a range of correlations for pain scores between 24, 48, and 72 hours post-operatively. I present these sensitivity analyses briefly.

6. I did not pursue more-elaborate analyses including but not limited to bivariate meta-analyses of mean pain VAS scores and the cumulative dose of oral morphine equivalents. Such analyses would help explore the impact on results of differences across trials in supplemental post-operative analgesia.

7. I did not apply adjustments for multiple tests, i.e., I did not use 99% confidence intervals or a Bonferroni–Holm correction, because they are not recommended for meta-analysis. The Hussain Study also did not apply such corrections for differences in the AUC, but for different reasons (because it was their primary outcome).

8. I have not yet checked or re-analyzed any of the secondary outcomes.

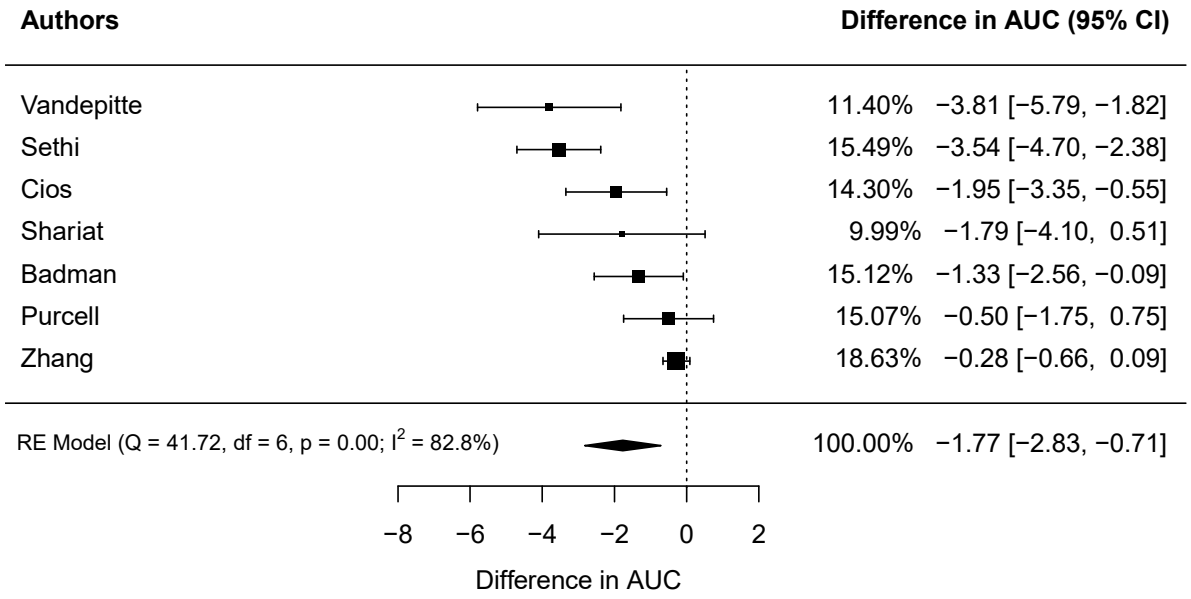
9. I did not yet check or re-assess the Hussain Study's Risk of Bias assessments for the included trials.

10. Because this note abstracts technical work, I do not expand on technical details and do not provide data or computational code.

Thus, there may be additional remarkable observations upon a more-thorough re-analysis of the Hussain Study.

My analysis of result from seven trials (authors Vandepitte, Sethi, Cios, Shariat, Badman, Purcell, Zhang[29]) estimates a meta-analysis mean for the difference in AUC of 1.77 cm*days (95% Confidence Interval [CI]: 0.71 to 2.83) favoring liposomal bupivacaine. This result is different than the estimate from the crude pooling analysis of the Hussein Study, which was 1.0 cm*day (95% CI 0.5 to 1.6), also favoring liposomal bupivacaine.

The Figure below is a *meta-analysis forest plot*. It depicts the results of the individual studies and the random-effects meta-analysis summary. The difference in the AUC of each study is shown by a black square (which denotes the point estimate) and a horizontal line (which denotes the 95% CI for the point estimate). The sizes of the black squares correspond to the proportional weight that trials received in the meta-analysis. For example, the AUC difference in Shariat has the largest variance (it has the widest 95% CI) and is the least precise; it received the smallest weight of 9.99% and is shown with the smallest square. Conversely, Zhang, has the smallest variance and receives the most weight of 18.63%. The dashed line at 0 is the line of no effect. The points plotted to the left of 0 correspond to negative numbers, which favor liposomal bupivacaine over nonliposomal bupivacaine.[30]



Because of the substantial clinical and methodological diversity in the characteristics of these trials, a random-effects meta-analysis model is used. A random-effects model allows for between-studies variance in the true study-specific AUC differences, estimates its magnitude,

[29] The publication by Zhang, in Chinese, and a machine translation were provided to me by counsel. I have not had the study report translated.

[30] A larger AUC corresponds to worse pain scores between 24 and 72 hours post-operatively. The difference in the AUC in each trial is the AUC with liposomal bupivacaine minus the AUC with nonliposomal bupivacaine. A negative difference means that the AUC with liposomal bupivacaine is smaller than the AUC with nonliposomal bupivacaine, i.e., the liposomal bupivacaine does better.

and incorporates it in the calculations. In this case, the clinical and methodological diversity in the trials manifests as differences in the trials' results. Some quantification is offered by the I^2 statistic that quantifies the extent of statistical heterogeneity. Here it is about 83%, which suggests that the results of the trials are diverse. The visual impression of the forest plot also conveys the same idea: Although the point estimates for the difference in AUC in all studies are in the direction that favors liposomal bupivacaine over nonliposomal bupivacaine, the magnitude of the difference varies across studies. Some studies show larger differences in favor of liposomal bupivacaine (e.g., Vandepitte and Sethi show point estimates better by 3.5 cm*days) and some show smaller (e.g., Purcell, at about 0.50 cm*days and Zhang at about 0.28 cm*days).

The clinical and methodological diversity between the trials makes the summary meta-analysis result challenging to interpret for clinical practice: The meta-analysis mean difference in the AUC (1.77 [95%: CI 0.71 to 2.83]) is the average effect in the observed trials. But these trials enrolled very different patients, and thus the meta-analysis mean is not the effect expected in a new patient. We should strive to gain some understanding about how, and possibly why, the results differ across trials. This is the focus of the heterogeneity analyses below.

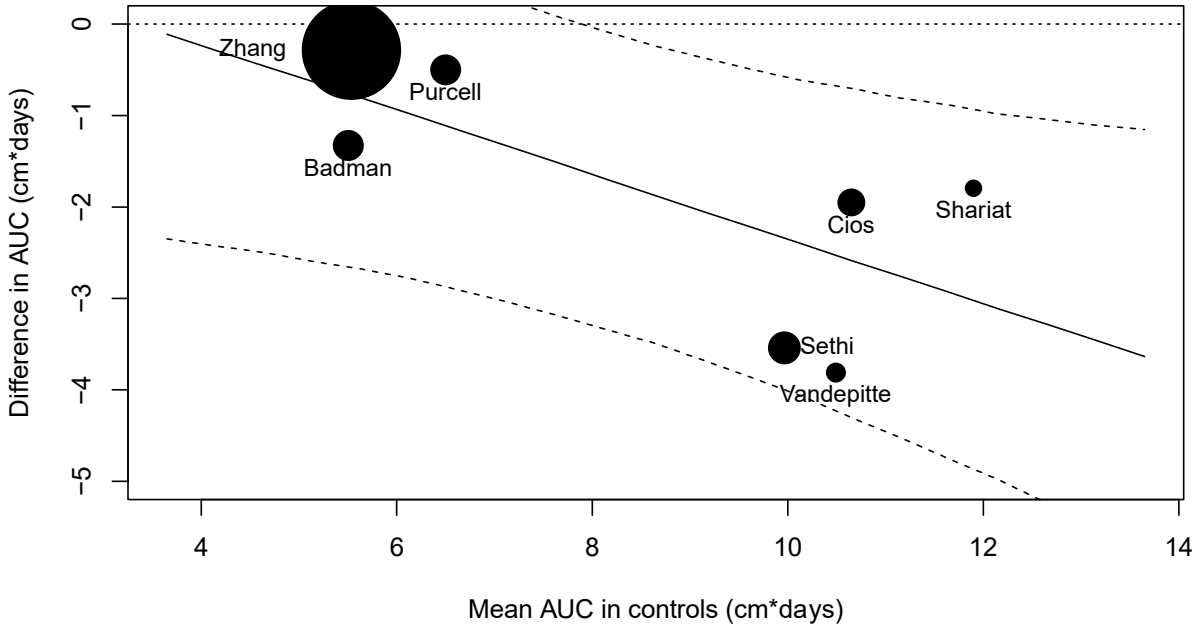
Example heterogeneity analyses

The goal of a heterogeneity analysis is to assess how treatment effects differ across trials, and if possible, propose explanations for any differences. I describe a basic heterogeneity analysis that seeks to answer the question: "Does the difference in the AUC in each trial depend on the amount of pain patients experience in each trial?" This analysis is a common starting point in most meta-analyses. The rationale is simple: Pain scores (which form the basis for the AUCs) are measured on a scale of 0–10. If a trial is done in patients who experience low pain scores (e.g., because the surgery is not very painful or patients received effective post-operative analgesia), then there is little opportunity to see a difference between liposomal bupivacaine and nonliposomal bupivacaine. By contrast, in trials in which patients experience high pain scores and there is a genuine difference in pain scores between the interventions, there may be more opportunity to see that difference.

The figure below shows the result of a control-response meta-regression analysis.[31] The difference in the AUC in each trial is shown on the vertical axis. The mean AUC in the controls, which represents the pain levels experienced by patients in a trial, is shown on the horizontal

[31] In this type of meta-regression, the response (treatment effect of difference in the AUC) is a function of the predictor (AUC in the nonliposomal bupivacaine controls) and response and predictor are naturally correlated across studies, which must be accounted for in a specialized analysis. I conducted the correct analysis in the Bayesian framework using standard numerical methods (Markov Chain Monte Carlo [MCMC]). I used three MCMC chains, with an adaptation of 5000 iterations and a burn-in of 10000 iterations. I used noninformative prior distributions for hyperparameters. Convergence was assessed visually and with the Brook-Gelman-Rubin diagnostic. Posterior inferences are based on 50000 samples from the joint posterior distribution and as described as medians and 95% highest posterior density Credible Intervals (95% CrI). The 95% Credible Intervals are the Bayesian analogue of the 95% Confidence Intervals.

axis. The black line that slopes downwards is the meta-regression evidence synthesis, and the dashed lines above and below it are the 95% Credible Intervals for the black line. Trials are shown as black circles with size proportional to the weight the trial receives in the meta-regression. The meta-regression analysis suggests that that for every 1 cm*day unit worsening in the AUC in the controls, the difference in the AUC becomes more favorable for liposomal bupivacaine by 0.35 cm*day (95% Credible Interval, 0.02, 0.61). Thus, it indicates that *when patients are in more pain (e.g., because of more painful surgeries or less effective post-operative analgesia), the effect of liposomal bupivacaine becomes larger*.



I also conducted a subgroup analysis by looking at whether the AUC in the controls was above (Subgroup A) or below (Subgroup B) 8.6 cm*day, which is the arithmetic average of the AUCs with nonliposomal bupivacaine across trials. The result is shown below.

Analysis	***Number of trials***	***Difference in AUC, random effects meta-analysis mean (95% CI)***	***P value for statistical heterogeneity (I^2, %)***	***Difference of subgroup A vs B (95% CI)***
Subgroup A: Mean AUC in the controls more than 8.6 cm*day	4	-2.85 (-3.87, -1.84)	0.28 (25)	-2.33 (-3.43, -1.22)
Subgroup B: Mean AUC in the controls less than 8.6 cm*day	3	-0.49 (-1.03, 0.05)	0.20 (36)	
All trials (no subgrouping)	7	-1.77 (-2.83, -0.71)	<0.001 (83)	Not applicable

Note that this subgroup analysis, which separates the trials by the mean AUC in the controls, appears to explain the between-studies statistical heterogeneity. When all trials are considered

together, the between-studies heterogeneity is large (I^2=83%); however, within each subgroup there is limited evidence for statistical heterogeneity (I^2 values are well below 50% in both subgroups A and B). This subgrouping of the trials explains most of the observed statistical heterogeneity in the meta-analysis.

Interpretation and a generated hypothesis: The meta-regression and subgroup analyses help formulate the clinically remarkable hypothesis that that *the treatment effect of liposomal bupivacaine is larger among patients who are in more pain*. Additional research is needed to confirm, but the analysis I have conducted to date, based on the trials identified by the Study authors, suggests this hypothesis to be true.

Example sensitivity analyses

I describe two sensitivity analyses. The first is a general sensitivity analysis that should be done in every meta-analysis to explore the dependence of the results on a single study. The second is important to assess the robustness of my re-analysis of the difference in the AUCs to values of the missing correlations for the pain scores at different time points.

Leave-one-out sensitivity analysis: Some additional insight is afforded by a leave-one out sensitivity analysis, where one excludes one trial at a time to explore the dependence of the meta-analysis on individual trials' results. This is a standard sensitivity analysis that is encouraged in all meta-analyses. The table below shows the results of the meta-analysis when dropping the trial in the first column.

Excluding this study:	***Difference in AUC, random effects meta-analysis mean (95% CI)***	***P value for statistical heterogeneity (I^2, %)***
Vandepitte	-1.5 (-2.54, -0.45)	<0.001 (82)
Sethi	-1.38 (-2.34, -0.42)	0.002 (73)
Cios	-1.76 (-3.00, -0.52)	<0.001 (86)
Shariat	-1.78 (-2.97, -0.59)	<0.001 (86)
Badman	-1.87 (-3.11, -0.62)	<0.001 (85)
Purcell	-2.00 (-3.17, -0.83)	<0.001 (83)
Zhang	-2.10 (-3.17, -1.03)	0.005 (68)

This shows that the result is somewhat sensitive to which study is excluded. All analyses favor liposomal bupivacaine, with point estimates for the difference in AUC ranging between 1.38 cm*day, when Sethi is excluded, and 2.10 cm*day, when Zhang is excluded.

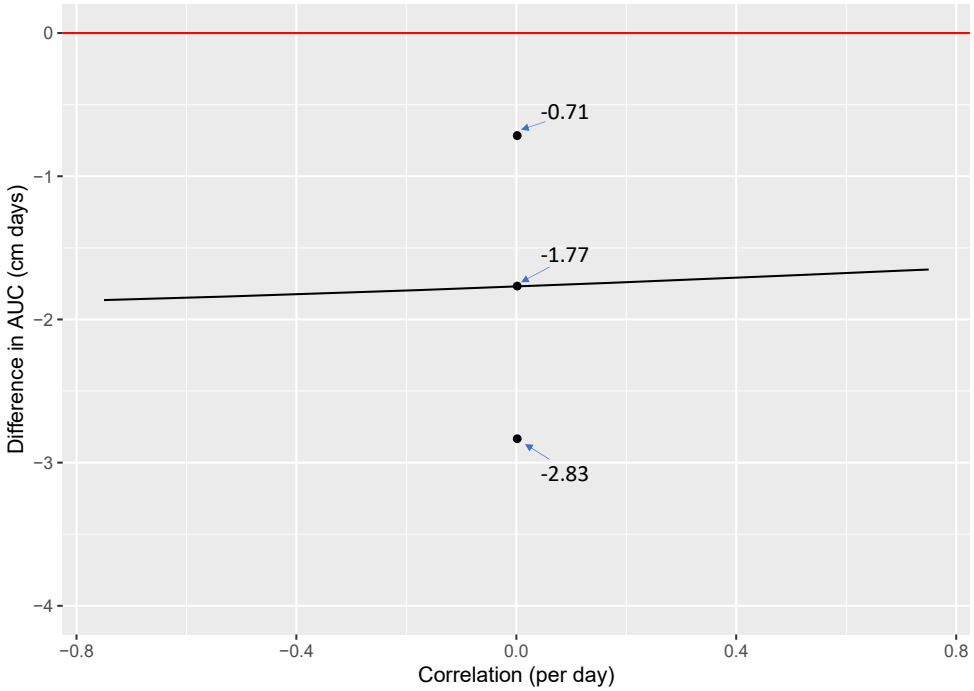
In general, the meta-analysis result remains statistically heterogeneous no matter which study is dropped in the sensitivity analysis. Regardless of the excluded study, the P values for heterogeneity remain less than 0.10 (the usual threshold for identifying statistical heterogeneity) and I^2 values exceed 50%.

Sensitivity analysis of the impact of pain score correlations across timepoints: The following is a form of sensitivity analysis one should do when some necessary information is not reported in the trials. I used the multivariate delta method to derive the difference in the AUC between

liposomal and nonliposomal bupivacaine in each study and its variance. The derivation requires the correlations between the mean pain scores at 24, 48, and 72 hours post-operatively in each treatment arm of each study. The main analysis, as well as the leave-one-out meta-analysis, assumed that the mean pain scores across the three time points are not correlated (have zero correlation). However, it is unclear how this assumption affects the results. To assess the impact of missing correlations, I specify a single parameter auto-correlation matrix for the mean pain scores of the form

$\mathbf{R} = \begin{bmatrix} 1 & \rho & \rho^2 \\ \rho & 1 & \rho \\ \rho^2 & \rho & 1 \end{bmatrix}$, where ρ is assumed to take values between -0.75 (a relatively large negative value) and 0.75 (a relatively large positive value).[32] A better range of ρ can be informed empirically, e.g., by getting information from the authors of each study. The following graph shows the meta-analysis random-effects mean difference in the AUC for the 6 trials with analyzable data, assuming different values for the day-to-day correlation in pain scores. The black line is the meta-analysis point estimate, and the blue ribbon is the width of the meta-analysis 95% confidence interval. The results of the main analysis (-1.77 [95% CI, -2.83 to -0.71]) are also depicted at correlation equals 0 ($\rho = 0$). This analysis suggests that the results of my main analyses would not change dramatically If I were to assume a different value for the correlation ρ. No such exploration is reported in the Hussain Study.

[32] Other structures for the correlation matrix $\mathbf{R}$ can be examined; e.g., a compound symmetry matrix or an unstructured matrix. A positive correlation in pain scores between two time points means that patients with higher scores at one time point will also tend to have higher scores at other time points. Negative correlations could also be observed— patients who have higher scores on one day could have lower scores on the next day, e.g., if the increased pain resulted in their getting supplemental medications to control their post-op pain and continued them on the next day.



Conclusion

Based on the above analyses:

1. I conclude that the foundational errors in the Hussain Study resulted in an unsound and deeply flawed analysis for the primary outcome (AUC differences regarding pain scores between 24 and 72 hours post-operatively). The re-analysis for the difference in the AUC with liposomal bupivacaine versus nonliposomal bupivacaine gives discordant results from those reported in the Hussain Study. This is troubling, irrespective of the direction in which the results change.

2. The re-analysis of seven trials with extractable data finds a mean difference in AUC between 24 and 72 hours post-operatively of 1.77 cm*days (95% CI, 0.71 to 2.83) favoring liposomal bupivacaine over nonliposomal bupivacaine (i.e., an average 1.77 point improvement on the pain scale), but with substantial statistical heterogeneity. This magnitude is on the order of the Hussain Study's threshold for clinical importance (which was set at 2.0 cm*days).

3. Heterogeneity analyses suggest that the treatment effect of liposomal bupivacaine versus nonliposomal bupivacaine becomes 0.35 cm*day (95% CrI: 0.02 to 0.61) larger for every 1 cm*day increase in the mean AUC in the controls (nonliposomal bupivacaine).

4. In additional heterogeneity analyses, in the subgroup of trials where the control group patients had a mean AUC of at least 8.6 cm*day (the mean value of the seven trials in my analysis), the AUC with liposomal bupivacaine was better by 2.85 cm*day (95% CI, 1.84 to 3.87) than that of nonliposomal bupivacaine. For trials where the mean AUC in the controls was less than 8.6 cm*day, the difference in the AUC was 0.49 cm*day (95% CI, -0.05 to 1.03) in favor of liposomal bupivacaine. This subgrouping appears to explain the between-studies statistical heterogeneity.

5. Thus, I conclude that:

    a. There is strong evidence that liposomal bupivacaine is more effective than nonliposomal bupivacaine in terms of the AUC metric for pain between 24 and 72 hours post-operatively.

    b. There is low to moderate strength of evidence that the treatment effect of liposomal bupivacaine is larger in studies with higher pain scores in the controls, as measured by higher AUCs with nonliposomal bupivacaine between 24 and 72 hours. The strength of the evidence is moderate because the result is based on a meta-regression analysis.

    c. There is low strength of evidence that in trials with higher pain scores in the controls, the improvement in the AUC is clinically important using a threshold of 2.0 cm*day. The strength of evidence is low because of imprecision and because the result is from a subgroup analysis.

    d. There is low strength of evidence that the level of pain experienced by patients in each trial explains the heterogeneity in trial results.

6. Finally, the Hussain Study contains methodological errors and inaccuracies that cast doubt on the correctness, completeness, and rigor of other analyses therein, the accuracy of their reporting, and the fairness of their interpretation and contextualization for clinical practice. Thus, a careful and detailed re-analysis of the Hussain Study may uncover different or additional observations, which may further change conclusions.

Date: ____April 8, 2021____

Thomas A. Trikalinos, M.D., Ph.D.

EXHIBIT A

TA Trikalinos

Center for Evidence Synthesis in Health
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Contents

Personal Information

Name, Position, Academic Departments

Name **Thomas A. Trikalinos**.

Position Professor

Departments Health Services, Policy & Practice (primary) and Biostatistics (secondary), Brown University School of Public Health

Other Director, Center for Evidence Synthesis in Health [*former Center for Evidence-based Medicine*], Brown University School of Public Health

Business Address

Address 121 S Main St, Providence, RI 02912, USA

Education

2006 **Ph.D. Epidemiology**, University of Ioannina, Ioannina, Greece.

Ph.D. Thesis *Diagnostic Procedures in Genetic Meta-analysis*

2002 **MD**, University of Ioannina, Ioannina, Greece.

Appointments

Academic Appointments

I was elected at my first academic appointment as Assistant Professor of Medicine at Tufts University in 2002, right after completing medical school in Greece. I moved to the US from Greece in 2006, after finishing my PhD.

2020– **Professor of Biostatistics**, School of Public Health, Brown University, Providence, RI 02912.

2020– **Professor of Health Services, Policy & Practice**, School of Public Health, Brown University, Providence, RI 02912.

2012–2020 **Associate Professor of Health Services, Policy & Practice**, School of Public Health, Brown University, Providence, RI 02912.

2012– **Adjunct Associate Professor of Medicine**, School of Medicine, Tufts University, Boston, MA 02111.

2012– **Adjunct Associate Professor of Clinical and Translational Science**, Clinical and Translational Science Institute, Tufts University, Boston, MA 02111.

Fall 2016 **Visiting scholar (on sabbatical from Brown U)**, Sloan School of Management and Operations Research Center, MIT, Cambridge, MA 02142.

2012–2013 **Visiting Associate Professor in Computer Science**, School of Engineering, Tufts University, Medford, MA 02155.

2002–2012 **Assistant Professor of Medicine**, School of Medicine, Tufts University, Boston, MA 02111.

2006–2007 **Postdoctoral Research Associate**, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

Professional Appointments

Brown University

2012– **Director**, Center for Evidence Synthesis in Health (*former Center for Evidence-based Medicine*), School of Public Health, Brown University.
Providence, RI 02912

Tufts Medical Center

2007–2012 **Special and Scientific Staff**, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

2006–2007 **Research Associate**, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

ICRHPS *[ICRHPS = Institute for Clinical Research and Health Policy Studies at Tufts Medical Center]*

2009–2012 **Co-Director**, Tufts Evidence-based Practice Center, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

2009–2012 **Associate Director**, Center for Clinical Evidence Synthesis, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

2008–2009 **Associate Director**, Tufts Evidence-based Practice Center, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

2007–2008 **Assistant Director**, Tufts Evidence-based Practice Center, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111.

Companies

Mycenean A 501 (c) (3) non-profit company incorporated in Rhode Island. It serves as an impartial custodian of open source software for evidence synthesis, shares data, disseminates information, provides education, training and consulting services in Evidence Synthesis.

2017– **Chief Executive Officer**.

Honors & Awards

1996 Competed for Greece in the 28th International Chemistry Olympiad in Moscow, Russia.

1996 Third National Prize in the annual National Chemistry Competition (organized by the National Chemists' Society). Member of the National Chemistry Team of Greece for 1995–1996.

1996 Second National Prize in the annual National Physics Competition (organized by the National Physicists' Society). Member of the National Physics Team of Greece for 1995–1996.

Membership in Societies

I list only active memberships. Refer to *Service, Professional Societies* for positions held.

Groups with elected membership

–Society for Research Synthesis Methodology (SRSM). SRSM has a cap of 85 active members.

Groups with open membership

–Society for Medical Decision Making (SMDM)

–American Statistical Association (ASA)

–The Institute for Operations Research and the Management Sciences (INFORMS)

Leadership Positions

2013–2016 **Secretary**, Society for Research Synthesis Methodology

2013 **Local Organizing CoChair** (with CH Schmid & J Lau), 2013 annual meeting of the Society for Research Synthesis Methodology

Other Roles

2014 **Member**, Senior Program Committee, AAAI Workshop on Modern Artificial Intelligence for Health Analytics. Association for the Advancement of Artificial Intelligence Conference, 27/07/2014, Quebec City, Canada.

University Service

Brown University

Standing Committees, Campus

2014–2016 **Member**, Research Advisory Board

2013–2016 **Member**, Graduate Council

Ad hoc Committees, Campus

2012 **Member**, Search Committee for the Vice President for Research

Ad hoc Committees, School of Public Health

2013–2014 **Member**, Mentorship Committee

2014 **Chair**, Search Committee for open rank position in Health Services, Policy & Practice (Research Track)

2015 **Member**, Search Committee for open rank position in Biostatistics (Tenure Track)

2015 **Member**, Promotion Committee for faculty in Epidemiology (Research Track)

2015 **Chair**, Promotion Committee for faculty in Health Services, Policy & Practice (Research Track)

2016 **Chair**, Search Committee for open rank position in Health Services, Policy & Practice (Research Track)

2016 **Member**, Search Committee for open rank position in Health Services, Policy & Practice (Tenure Track)

2016 **Member**, Diversity and Inclusion Plan for the School of Public Health; Professional Development and Programming Group

2017 **Member**, Search Committee for open rank position in Health Services, Policy & Practice (Research Track)

2017 **Member**, Committee for Appointment of an Adjunct Professor in Health Services, Policy & Practice (Research Track)

Tufts University

2011–2012 **Chair**, Scientific Affairs Committee, School of Medicine

2008–2011 **Member**, Scientific Affairs Committee, School of Medicine

Tufts Medical Center

2009–2012 **Member**, Executive Committee, Institute for Clinical Research and Health Policy Studies

2008–2009 **Member**, Infrastructure Committee, Institute for Clinical Research and Health Policy Studies

University of Ioannina, Greece

2015 **International Member**, Promotion Committee for a tenured Associate Professor Position in Epidemiology, Department of Hygiene and Epidemiology, School of Medicine

University of Applied Sciences of Thessaly, Greece

2017 **International Alternate Member**, Committee for choosing tenure-track faculty (Assistant Professor rank) in Public Health with emphasis on vaccines, Department of Medical Laboratories, School of Medical Professions

University of Thessaly, Greece

2015 **International Alternate Member**, Promotion Committee for a tenured Associate Professor Position in Bioinformatics and Biomathematics, Department of Bioinformatics and Biostatistics

National or International Service

Grant Application Review Boards

Ad hoc Member In 2013: Patient Centered Outcomes Research Institute (PCORI): Applications for Clinical Data Research Networks and Patient-Powered Research Networks

Ad hoc Member In 2017: National Institute for Allergies and Infectious Diseases (NIAID): ZAI1

Ad hoc Member In 2019: National Institute of Neuroological Disorders and Stroke: NST2

Editorial responsibilities

Editorial Board Member **Current:** *BMC Medical Research Methodology* (editorial advisor), *Research Synthesis Methods*; **Past:** *PLoS Currents – Evidence for Genomic Applications*

Journal Manuscript Reviewer

Peer Reviewer I regularly conduct peer review for many journals. The following is a non-exhaustive list: *Proceedings of the National Academies of Sciences, Journal of the American Medical Association, Statistics in Medicine, Annals of Internal Medicine, British Medical Journal, PLoS Medicine, Journal of the National Cancer Institute, Annals of Applied Statistics, Bioinformatics, Journal of Clinical Epidemiology, Trials, Medical Decision Making, BMC Medicine, BMC Medical Research Methodology, Cochrane Library of Systematic Reviews.*

National Panels & Workgroups

2017 **Member**, National Science Foundation (NSF) Smart and Connected Health (SCH) Program Visioning Meeting, advising the NSF on the research funding priorities of next 5 years of the SCH Program

2013–2015 **Member**, Technical Expert Panel, advising the US Preventive Services Task Force on methodology

International Organizations

World Health Organization

2016 **Co-Chair**, Conference on using modeling to inform global guidelines. 27-29 April 2016.

GAPPNet In 2009, I was a member of the Knowledge Synthesis Workgroup and of the Dissemination Workgroup, Genomic Applications in Practice and Prevention Networking (GAPPNet) Initiative. This initiative aims to accelerate and streamline effective and responsible use of validated and useful genomic knowledge and applications, such as genetic tests, technologies, and family history, into clinical and public health practice. It is supported by the Centers for Disease Control Public Health Genomics Office.

Publications

According to Thompson ISI, as of March 9, 2020:

–Over 11,000 citations.

–$h = 47$, that is, 47 of my papers have received at least as many citations.

–$m = 2.6$. The m index normalizes the h index by the years of one's scientific production.

–Self-citation rate is 166/11200 (1.5%). The h and m indices remain practically unchanged after excluding self-citations.

According to Google Scholar, as of March 9, 2020:

–Over 21,000 citations.

–$h = 63$

–$m = 3.5$

Books & Monographs

None

Chapters in Books

1. **Trikalinos TA**, Ioannidis JP (2005) Assessing the evolution of effect sizes over time. *In* Publication bias – Prevention, Assessment and Adjustments, Wiley, chapter 13.

2. Wallace BC, Dahabreh IJ, Lau J, Schmid CH, **Trikalinos TA** (2014) Modernizing evidence synthesis for Evidence-based Medicine. *In* Clinical Decision Support, Elsevier, chapter 12.

3. Neumann PJ, Sanders-Schmidler G, Basu A, Brock D, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA, Sculpher MJ, **Trikalinos TA**, Siegel JE, Russell LB, Ganiats TG (2016) Recommendations on perspectives for the Reference Case. *In* Cost-Effectiveness in Health and Medicine, Oxford, chapter 3.

4. Kuntz KM, Russell LB, Owens DK, Sanders-Schmidler GD, **Trikalinos TA**, Salomon JA (2016) Decision models in cost-effectiveness analysis. *In* Cost-Effectiveness in Health and Medicine, Oxford, chapter 5.

5. **Trikalinos TA**, Russell LB, Sanders-Schmidler GD (2016) Evidence synthesis for informing cost-effectiveness analysis. *In* Cost-Effectiveness in Health and Medicine, Oxford, chapter 9.

6. Salomon JA, **Trikalinos TA**, Sanders-Schmidler GD, Mandelblatt JS (2016) Identifying and quantifying the consequences of interventions. *In* Cost-Effectiveness in Health and Medicine, Oxford, chapter 6.

7. Dahabreh IJ, **Trikalinos TA**, Kent DM, Schmid CH (2017) Heterogeneity of treatment effects in comparative effectiveness research. *In* Methods in Comparative Effectiveness Research, Chapman and Hall/CRC, chapter 8.

8. Lau J, Morton SC, Schmid CH, **Trikalinos TA** (2017) Systematic reviews in comparative effectiveness research. *In* Methods in Comparative Effectiveness Research, Chapman and Hall/CRC, chapter 10.

Refereed Journal Articles

1. Adam GP, Balk EM, Jap J, Senturk B, Sanders-Schmidler G, Lallinger K, Butler M, Brasure M, **Trikalinos TA** (2019) AHRQ EPC Series on Improving Translation of Evidence: Web-Based Interactive Presentation of Systematic Review Reports. Jt Comm J Qual Patient Saf 45: 629–638.

2. Rönn MM, Menzies NA, Gift TL, Chesson HW, **Trikalinos TA**, Bellerose M, Malyuta Y, Berruti A, Gaydos CA, Hsu KK, Salomon JA (2019) Potential for Point-of-Care Tests to Reduce Chlamydia-associated Burden in the United States: A Mathematical Modeling Analysis. Clin Infect Dis .

3. Jones HE, Gatsonis CA, **Trikalinos TA**, Welton NJ, Ades AE (2019) Quantifying how diagnostic test accuracy depends on threshold in a meta-analysis. Stat Med 38: 4789–4803.

4. Savitz DA, Wellenius GA, **Trikalinos TA** (2019) The problem with mechanistic risk of bias assessments in evidence synthesis of observational studies and a practical alternative: Assess the impact of specific sources of potential bias. Am J Epidemiol (Epub ahead of print).

5. Bertsimas D, Dunn J, Steele DW, **Trikalinos TA**, Wang Y (2019) Comparison of machine learning optimal classification trees with the Pediatric Emergency Care Applied Research Network head trauma decision rules. JAMA Pediatr (Epub ahead of print).

6. Soboczenski F, **Trikalinos TA**, Kuiper J, Bias RG, Wallace BC, Marshall IJ (2019) Machine learning to help researchers evaluate biases in clinical trials: a prospective, randomized user study. BMC Medical Informatics and Decision Making 19: 96.

7. Balk EM, Adam GP, Corsi K, Mogul A, **Trikalinos TA**, Jeppson PC (2019) Adverse events associated with nonsurgical treatments for urinary incontinence in women: a systematic review. J Gen Intern Med (Epub ahead of print).

8. Balk EM, Gazula A, Markozannes G, Kimmel HJ, Saldanha IJ, **Trikalinos TA**, Resnik LJ (2019) Psychometric properties of functional, ambulatory, and quality of life instruments in lower limb amputees: a systematic review. Arch Phys Med Rehabil (Epub ahead of print).

9. Balk EM, Rofeberg VN, Adam GP, Kimmel HJ, **Trikalinos TA**, Jeppson PC (2019) Pharmacological and non-pharmacological treatments for urinary incontinence in women: A systematic review and network meta-analysis of clinical outcomes. Annals of Internal Medicine (Epub ahead of print).

10. Zgodic A, Schmid CH, Olkin I, **Trikalinos TA** (2019) Different evidence-summaries have implications for contextualizing findings of meta-analysis of diagnostic tests. Journal of Clinical Epidemiology 109: 51–61.

11. Kim DD, **Trikalinos TA**, Wong JB (2019) Leveraging cumulative network meta-analysis and value of information analysis to understand the evolving value of medical research. Med Decis Making 39: 119–129.

12. Neumann PJ, Kim DD, **Trikalinos TA**, Sculpher MJ, Salomon JA, Prosser LA, Owens DK, Meltzer DO, Kuntz KM, Krahn M, Feeny D, Basu A, Russell LB, Siegel JE, Ganiats TG, Sanders GD (2018) Future directions for cost-effectiveness analyses in health and medicine. Med Decis Making 38: 767-777.

13. Panagiotou OA, Markozannes G, Adam GP, Kowalski R, Gazula A, Di M, Bond DS, Ryder BA, **Trikalinos TA** (2018) Comparative Effectiveness and Safety of Bariatric Procedures in Medicare-Eligible Patients: A Systematic Review. JAMA Surg 153: e183326.

14. Kimmel HJ, Brice YN, **Trikalinos TA**, Sarkar IN, Ranney ML (2019) Real-time emergency department electronic notifications regarding high-risk patients: A systematic review. Telemed J E Health 25: 604–618.

15. Drucker AM, Adam GP, Rofeberg V, Gazula A, Smith B, Moustafa F, Weinstock MA, **Trikalinos TA** (2018) Treatments of primary basal cell carcinoma of the skin: A systematic review and network meta-analysis. Ann Intern Med 169: 456-466.

16. Adam GP, Springs S, **Trikalinos TA**, Williams JW, Eaton JL, Von Isenburg M, Gierisch JM, Wilson LM, Robinson KA, Viswanathan M, Middleton JC, Forman-Hoffman VL, Berliner E, Kaplan RM (2018) Does information from ClinicalTrials.gov increase transparency and reduce bias? Results from a five-report case series. Syst Rev 7: 59.

17. Adam GP, Di M, Cu-Uvin S, Halladay C, Smith BT, Iyer S, **Trikalinos TA** (2018) Strategies for improving the lives of US women aged 40 and above living with HIV/AIDS: An evidence map. Syst Rev 7: 25.

18. Bertsimas D, Silberholz JM, **Trikalinos TA** (2018) Optimal healthcare decision making under multiple mathematical models: Application in prostate cancer screening. Health Care Manag Sci 21: 105–118.

19. Tasillo A, Salomon JA, **Trikalinos TA**, Horsburgh CR, Marks SM, Linas BP (2017) Cost-effectiveness of testing and treatment for latent tuberculosis infection in residents born outside the United States with and without medical comorbidities in a simulation model. JAMA Intern Med 177: 1755–1764.

20. Steele DW, Adam GP, Di M, Halladay CH, Balk EM, **Trikalinos TA** (2017) Effectiveness of tympanostomy tubes for otitis media: a meta-analysis. Pediatrics 139.

21. Steele DW, Adam GP, Di M, Halladay CW, Balk EM, **Trikalinos TA** (2017) Prevention and treatment of tympanostomy tube otorrhea: a meta-analysis. Pediatrics 139.

22. Ellis AG, **Trikalinos TA**, Wessler BS, Wong JB, Dahabreh IJ (2018) Propensity score-based methods in comparative effectiveness research on coronary artery disease. Am J Epidemiol 187: 1064–1078.

23. Mortensen ML, Adam GP, **Trikalinos TA**, Kraska T, Wallace BC (2017) An exploration of crowdsourcing citation screening for systematic reviews. Res Synth Methods 8: 366–386.

24. Dahabreh IJ, **Trikalinos TA**, Lau J, Schmid CH (2017) Univariate and bivariate likelihood-based meta-analysis methods performed comparably when marginal sensitivity and specificity were the targets of inference. J Clin Epidemiol 83: 8–17.

25. Dahabreh IJ, Wong JB, **Trikalinos TA** (2017) Validation and calibration of structural models that combine information from multiple sources. Expert Rev Pharmacoecon Outcomes Res 17: 27–37.

26. Kapoor A, Ellis A, Shaffer N, Gurwitz J, Chandramohan A, Saulino J, Ishak A, Okubanjo T, Michota F, Hylek E, **Trikalinos TA** (2017) Comparative effectiveness of venous thromboembolism prophylaxis options for the patient undergoing total hip and knee replacement: a network meta-analysis. J Thromb Haemost 15: 284–294.

27. Dahabreh IJ, **Trikalinos TA**, Balk EM, Wong JB (2016) Recommendations for the conduct and reporting of modeling and simulation studies in health technology assessment. Ann Intern Med 165: 575–581.

28. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA, Sculpher MJ, **Trikalinos TA**, Russell LB, Siegel JE, Ganiats TG (2016) Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses in health and medicine: the second panel on cost-effectiveness in health and medicine. JAMA 316: 1093-1103.

29. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, Altman DG, Booth A, Chan AW, Chang S, Clarke M, Clifford T, Dickersin K, Egger M, Ghersi D, Goetzsche PC, Grimshaw JM, Groves T, Helfand M, Higgins J, Lasserson T, Lau J, Liberati A, Lohr K, McGowan J, Moher D, Mulrow C, Norton M, Page M, Petticrew M, Sampson M, Schunemann H, Shamseer L, Shekelle P, Simera I, Stewart LA, Summerskill W, Tetzlaff J, **Trikalinos TA**, Tovey D, Turner L, Whitlock E (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 4: 1.

30. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, Altman DG, Booth A, Chan AW, Chang S, Clarke M, Clifford T, Dickersin K, Egger M, Ghersi D, G?tzsche PC, Grimshaw JM, Groves T, Helfand M, Higgins J, Lasserson T, Lau J, Liberati A, Lohr K, McGowan J, Moher D, Mulrow C, Norton M, Page M, Petticrew M, Sampson M, Schunemann H, Shamseer L, Shekelle P, Simera I, Stewart LA, Summerskill W, Tetzlaff J, **Trikalinos TA**, Tovey D, Turner L, Whitlock E (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 349: g7647.

31. Halladay CW, **Trikalinos TA**, Schmid IT, Schmid CH, Dahabreh IJ (2015) Using data sources beyond PubMed has a modest impact on the results of systematic reviews of therapeutic interventions. J Clin Epidemiol 68: 1076–1084.

32. Dahabreh IJ, Steele DW, Shah N, **Trikalinos TA** (2015) Oral mechanical bowel preparation for colorectal surgery: systematic review and meta-analysis. Dis Colon Rectum 58: 698–707.

33. Ott BR, Daiello LA, Dahabreh IJ, Springate BA, Bixby K, Murali M, **Trikalinos TA** (2015) Do statins impair cognition? A systematic review and meta-analysis of randomized controlled trials. J Gen Intern Med 30: 348–358.

34. Olkin I, **Trikalinos TA** (2015) Constructions for a bivariate beta distribution. Statistics & Probability Letters 96: 54–60.

35. **Trikalinos TA**, Hoaglin DC, Small KM, Terrin N, Schmid CH (2014) Methods for the joint meta-analysis of multiple tests. Research Synthesis Methods 5: 294–312.

36. Guise JM, Chang C, Viswanathan M, Glick S, Treadwell J, Umscheid CA, Whitlock E, Fu R, Berliner E, Paynter R, Anderson J, Motu'apuaka P, **Trikalinos TA** (2014) Agency for Healthcare Research and Quality Evidence-based Practice Center methods for systematically reviewing complex multicomponent health care interventions. J Clin Epidemiol 67: 1181–1191.

37. Kelly MJ, **Trikalinos TA**, Dahabreh IJ, Gianferante M, Parsons SK (2014) Cranial radiation for pediatric T-lineage acute lymphoblastic leukemia: A systematic review and meta-analysis. Am J Hematol 89: 992–997.

38. Wallace BC, Paul MJ, Sarkar U, **Trikalinos TA**, Dredze M (2014) A large-scale quantitative analysis of latent factors and sentiment in online doctor reviews. J Am Med Inform Assoc 21: 1098–1103.

39. Riley RD, Takwoingi Y, **Trikalinos TA**, Guha A, Biswas A, Ensor J, Morris RK, Deeks JJ (2014) Meta-analysis of test accuracy studies with multiple and missing thresholds: a multivariate-normal model. J Biometrics Biostat 5.

40. Jansen JP, **Trikalinos TA**, Cappelleri JC, Daw J, Andes S, Eldessouki R, Salanti G (2014) Indirect treatment comparison/network meta-analysis study questionnaire to assess relevance and credibility to inform health care decision making: An ISPOR-AMCP-NPC Good Practice Task Force report. Value Health 17: 157–173.

41. **Trikalinos TA**, Hoaglin DC, Schmid CH (2014) An empirical comparison of univariate and multivariate meta-analyses for categorical outcomes. Stat Med 33: 1141–1159.

42. Wallace BC, Barton LM, Small K, Wilson IB, **Trikalinos TA** (2014) Automatically annotating topics in transcripts of patient-provider interactions via machine learning. Med Decis Making 34: 503–512.

43. **Trikalinos TA**, Segal JB, Boyd CM (2014) Addressing multimorbidity in evidence integration and synthesis. J Gen Intern Med 29: 661–669.

44. Schmid CH, **Trikalinos TA**, Olkin I (2014) Bayesian network meta-analysis for unordered categorical outcomes with incomplete data. Research Synthesis Methods 5: 162–185.

45. Yu WW, Schmid CH, Lichtenstein AH, Lau J, **Trikalinos TA** (2013) Empirical evaluation of meta-analytic approaches for nutrient and health outcome dose-response data. Research Synthesis Methods 4: 256–268.

46. Dahabreh IJ, Chung M, Kitsios GD, Terasawa T, Raman G, Tatsioni A, Tobar A, Lau J, **Trikalinos TA**, Schmid CH (2013) Survey of the methods and reporting practices in published meta-analyses of test performance: 1987 to 2009. Research Synthesis Methods 4: 242–255.

47. Olkin I, Dahabreh IJ, **Trikalinos TA** (2012) GOSH – a graphical display of study heterogeneity. Research Synthesis Methods 3: 214–223.

48. Balk EM, Chung M, Chen ML, Chang LK, **Trikalinos TA** (2013) Data-extraction from machine translated versus original language randomized trials: A comparative study. Systematic Reviews 2: 97.

49. Dahabreh IJ, Schmid CH, Lau J, Varvarigou V, Murray S, **Trikalinos TA** (2013) Genotype misclassification in genetic association studies of the rs1042522 TP53 (Arg72Pro) polymorphism: a systematic review of studies of breast, lung, colorectal, ovarian, and endometrial cancer. Am J Epidemiol 177: 1317–1325.

50. Wallace BC, Dahabreh IJ, Schmid CH, Lau J, **Trikalinos TA** (2013) Modernizing the systematic review process to inform comparative effectiveness: tools and methods. J Comparative Effectiveness Res 2: 273–282.

51. Wallace BC, Dahabreh IJ, **Trikalinos TA**, Lau J, Trow P, Schmid CH (2013) Closing the gap between methodologists and end-users: R as a computational back-end. J Stat Software 49: 1-15.

52. Koulouridis I, Alfayez M, **Trikalinos TA**, Balk EM, Jaber BL (2013) Dose of erythropoiesis-stimulating agents and adverse outcomes in chronic kidney disease: A metaregression analysis. Am J Kidney Dis 61: 44-56.

53. **Trikalinos TA**, Olkin I (2012) Meta-analysis of effect sizes reported at multiple time points: A multivariate approach. Clin Trials 9: 610-620.

54. Terasawa T, Trikalinos NA, Djulbegovic B, **Trikalinos TA** (2013) Comparative efficacy of first-line therapies for advanced-stage chronic lymphocytic leukemia: a multiple-treatment meta-analysis. Cancer Treat Rev 39: 340–349.

55. Dahabreh IJ, Sheldrick RC, Paulus JK, Chung M, Varvarigou V, Jafri H, Rassen JA, **Trikalinos TA**, Kitsios GD (2012) Do observational studies using propensity score methods agree with randomized trials? A systematic comparison of studies on acute coronary syndromes. Eur Heart J 33: 1893-1901.

56. **Trikalinos TA**, Balion CM, Coleman CI, Griffith L, Santaguida PL, Vandermeer B, Fu R (2012) Chapter 8: meta-analysis of test performance when there is a 'gold standard'. J Gen Intern Med 27 Suppl 1: 56–66.

57. **Trikalinos TA**, Balion CM (2012) Chapter 9: options for summarizing medical test performance in the absence of a 'gold standard'. J Gen Intern Med 27 Suppl 1: 67–75.

58. **Trikalinos TA**, Kulasingam S, Lawrence WF (2012) Chapter 10: deciding whether to complement a systematic review of medical tests with decision modeling. J Gen Intern Med 27 Suppl 1: 76–82.

59. Wallace BC, Small K, Brodley CE, Lau J, Schmid CH, Bertram L, Lill CM, Cohen JT, **Trikalinos TA** (2012) Toward modernizing the systematic review pipeline in genetics: efficient updating via data mining. Genet Med 14: 663–669.

60. Rodday AM, Triedman JK, Alexander ME, Cohen JT, Ip S, Newburger JW, Parsons SK, **Trikalinos TA**, Wong JB, Leslie LK (2012) Electrocardiogram screening for disorders that cause sudden cardiac death in asymptomatic children: a meta-analysis. Pediatrics 129: e999-e1010.

61. Chung M, Lee J, Terasawa T, Lau J, **Trikalinos TA** (2011) Vitamin D with or without calcium supplementation for prevention of cancer and fractures: an updated meta-analysis for the U.S. Preventive Services Task Force. Ann Intern Med 155: 827–838.

62. Dahabreh IJ, **Trikalinos TA**, Paulus JK (2012) Parity and risk of lung cancer in women: systematic review and meta-analysis of epidemiological studies. Lung Cancer 76: 150–158.

63. **Trikalinos TA**, Moorthy D, Chung M, Yu WW, Lee J, Lichtenstein AH, Lau J (2012) Concordance of randomized and nonrandomized studies was unrelated to translational patterns of two nutrient-disease associations. J Clin Epidemiol 65: 16–29.

64. Wessler BS, Kramer DG, Kelly JL, **Trikalinos TA**, Kent DM, Konstam MA, Udelson JE (2011) Drug and device effects on peak oxygen consumption, 6-minute walk distance, and natriuretic peptides as predictors of therapeutic effects on mortality in patients with heart failure and reduced ejection fraction. Circ Heart Fail 4: 578–588.

65. Rao M, Mottl AK, Cole SA, Umans JG, Freedman BI, Bowden DW, Langefeld CD, Fox CS, Yang Q, Cupples A, Iyengar SK, Hunt SC, **Trikalinos TA** (2012) Meta-analysis of genome-wide linkage scans for renal function traits. Nephrol Dial Transplant 27: 647–656.

66. Fu R, Gartlehner G, Grant M, Shamliyan T, Sedrakyan A, Wilt TJ, Griffith L, Oremus M, Raina P, Ismaila A, Santaguida P, Lau J, **Trikalinos TA** (2011) Conducting quantitative synthesis when

comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol 64: 1187–1197.

67. Dahabreh IJ, Terasawa T, Castaldi PJ, **Trikalinos TA** (2011) Systematic review: Anti-epidermal growth factor receptor treatment effect modification by KRAS mutations in advanced colorectal cancer. Ann Intern Med 154: 37–49.

68. Terasawa T, Dahabreh I, **Trikalinos TA** (2010) BCR-ABL mutation testing to predict response to tyrosine kinase inhibitors in patients with chronic myeloid leukemia. PLoS Curr 2: RRN1204.

69. Alsheikh-Ali AA, **Trikalinos TA**, Ruthazer R, Terrin N, Wong JB, Sarnak MJ, Estes NA, Kent DM (2011) Risk of arrhythmic and nonarrhythmic death in patients with heart failure and chronic kidney disease. Am Heart J 161: 204–209.

70. Kitsios GD, Dahabreh IJ, **Trikalinos TA**, Schmid CH, Huggins GS, Kent DM (2011) Heterogeneity of the phenotypic definition of coronary artery disease and its impact on genetic association studies. Circ Cardiovasc Genet 4: 58–67.

71. Dahabreh I, Terasawa T, Castaldi P, **Trikalinos TA** (2010) CYP2D6 testing to predict response to tamoxifen in women with breast cancer: Pharmacogenomic. PLoS Curr 2: RRN1176.

72. Dahabreh IJ, Kitsios GD, Kent DM, **Trikalinos TA** (2010) Paraoxonase 1 polymorphisms and ischemic stroke risk: a systematic review and meta-analysis. Genet Med 12: 606–615.

73. Kramer DG, **Trikalinos TA**, Kent DM, Antonopoulos GV, Konstam MA, Udelson JE (2010) Quantitative evaluation of drug or device effects on ventricular remodeling as predictors of therapeutic effects on mortality in patients with heart failure and reduced ejection fraction: a meta-analytic approach. J Am Coll Cardiol 56: 392–406.

74. Gabbay E, Calvo-Broce J, Meyer KB, **Trikalinos TA**, Cohen J, Kent DM (2010) The empirical basis for determinations of medical futility. J Gen Intern Med 25: 1083–1089.

75. Peter I, Crosier MD, Yoshida M, Booth SL, Cupples LA, Dawson-Hughes B, Karasik D, Kiel DP, Ordovas JM, **Trikalinos TA** (2011) Associations of APOE gene polymorphisms with bone mineral density and fracture risk: a meta-analysis. Osteoporos Int 22: 1199–1209.

76. Chung M, Balk EM, Ip S, Lee J, Terasawa T, Raman G, **Trikalinos TA**, Lichtenstein AH, Lau J (2010) Systematic review to support the development of nutrient reference intake values: challenges and solutions. Am J Clin Nutr 92: 273–276.

77. Pittas AG, Chung M, **Trikalinos TA**, Mitri J, Brendel M, Patel K, Lichtenstein AH, Lau J, Balk EM (2010) Systematic review: Vitamin D and cardiometabolic outcomes. Ann Intern Med 152: 307–314.

78. Wallace BC, **Trikalinos TA**, Lau J, Brodley C, Schmid CH (2010) Semi-automated screening of biomedical citations for systematic reviews. BMC Bioinformatics 11: 55.

79. Wallace BC, Schmid CH, Lau J, **Trikalinos TA** (2009) Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol 9: 80.

80. Castaldi PJ, Cho MH, Cohn M, Langerman F, Moran S, Tarragona N, Moukhachen H, Venugopal R, Hasimja D, Kao E, Wallace B, Hersh CP, Bagade S, Bertram L, Silverman EK, **Trikalinos TA** (2010) The COPD genetic association compendium: a comprehensive online database of COPD genetic associations. Hum Mol Genet 19: 526–534.

81. Ip S, Chung M, Raman G, **Trikalinos TA**, Lau J (2009) A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries. Breastfeed Med 4 Suppl 1: 17–30.

82. **Trikalinos TA**, Chung M, Lau J, Ip S (2009) Systematic review of screening for bilirubin encephalopathy in neonates. Pediatrics 124: 1162–1171.

83. Terasawa T, Dvorak T, Ip S, Raman G, Lau J, **Trikalinos TA** (2009) Systematic review: charged-particle radiation therapy for cancer. Ann Intern Med 151: 556–565.

84. **Trikalinos TA**, Siebert U, Lau J (2009) Decision-analytic modeling to evaluate benefits and harms of medical tests: uses and limitations. Med Decis Making 29: E22–29.

85. Djulbegovic B, **Trikalinos TA**, Roback J, Chen R, Guyatt G (2009) Impact of quality of evidence on the strength of recommendations: an empirical study. BMC Health Serv Res 9: 120.

86. Barza M, **Trikalinos TA**, Lau J (2009) Statistical considerations in meta-analysis. Infect Dis Clin North Am 23: 195–210.

87. **Trikalinos TA** (2009) Does it mean anything if your own name is wrong in your published paper? FASEB J 23: 2345–2348.

88. **Trikalinos TA**, Alsheikh-Ali AA, Tatsioni A, Nallamothu BK, Kent DM (2009) Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis. Lancet 373: 911–918.

89. Chung M, Balk EM, Ip S, Raman G, Yu WW, **Trikalinos TA**, Lichtenstein AH, Yetley EA, Lau J (2009) Reporting of systematic reviews of micronutrients and health: a critical appraisal. Am J Clin Nutr 89: 1099–1113.

90. Russell R, Chung M, Balk EM, Atkinson S, Giovannucci EL, Ip S, Lichtenstein AH, Mayne ST, Raman G, Ross AC, **Trikalinos TA**, West KP, Lau J (2009) Opportunities and challenges in conducting systematic reviews to support the development of nutrient reference values: vitamin A as an example. Am J Clin Nutr 89: 728–733.

91. Chung M, Raman G, **Trikalinos TA**, Lau J, Ip S (2008) Interventions in primary care to promote breastfeeding: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 149: 565–582.

92. Stefanis NC, **Trikalinos TA**, Avramopoulos D, Smyrnis N, Evdokimidis I, Ntzani EE, Hatzimanolis A, Ioannidis JP, Stefanis CN (2008) Association of RGS4 variants with schizotypy and cognitive endophenotypes at the population level. Behav Brain Funct 4: 46.

93. Alsheikh-Ali AA, **Trikalinos TA**, Kent DM, Karas RH (2008) Statins, low-density lipoprotein cholesterol, and risk of cancer. J Am Coll Cardiol 52: 1141–1147.

94. Papatheodorou SI, **Trikalinos TA**, Ioannidis JP (2008) Inflated numbers of authors over time have not been just due to increasing research complexity. J Clin Epidemiol 61: 546–551.

95. **Trikalinos TA**, Olkin I (2008) A method for the meta-analysis of mutually exclusive binary outcomes. Stat Med 27: 4279–4300.

96. Kent DM, **Trikalinos TA** (2008) Are 'treatment' bare metal stents superior to 'control' bare metal stents? A meta-analytic approach. Am Heart J 155: 624–629.

97. **Trikalinos TA**, Salanti G, Zintzaras E, Ioannidis JP (2008) Meta-analysis methods. Adv Genet 60: 311–334.

98. van Meurs JB, **Trikalinos TA**, Ralston SH, Balcells S, Brandi ML, Brixen K, Kiel DP, Langdahl BL, Lips P, Ljunggren O, Lorenc R, Obermayer-Pietsch B, Ohlsson C, Pettersson U, Reid DM, Rousseau F, Scollen S, Van Hul W, Agueda L, Akesson K, Benevolenskaya LI, Ferrari SL, Hallmans G, Hofman A, Husted LB, Kruk M, Kaptoge S, Karasik D, Karlsson MK, Lorentzon M, Masi L, McGuigan FE, Mellstrom D, Mosekilde L, Nogues X, Pols HA, Reeve J, Renner W, Rivadeneira F, van Schoor NM, Weber K, Ioannidis JP, Uitterlinden AG, Contopoulos-Ioannidis DG, Arp P, Jhamai M, van Leeuwen H, Albagha OM, Macdonald H, Stewart A, Bassiti A, Dunning AM, Carstens M, Stenkjaer L, Bofill NG, Tanini A, Falchetti A, Grinberg D, Bustamante M, Diez-Perez A, Mellibovsky L, Jurado S, Walter D, Hartl U, Gugatschka M, Bonelli C, Dobnig H, Fahrleitner-Pammer A, Karczmarewicz E, Pludowski P, Beckers S, Peeters A, Piters E, Balemans W, Svensson O, Nordstrom P, Nielsen TL, Wraae K, Bathum L, Brasen C, Hagen C, Andersen M, Abrahamsen B, Parsons C, Bear S, Farmer R, Jensen JE, Eiken P, Lukaszkiewicz J, Bilinski P, Czerwinski E, Lewinski A, Marcinowska-Suchowierska E, Milewicz A, Spaczynski M, Jaworski M, Nuti R, Grazio S, Miazgowski

T, Boonen SR, Masaryk P, Stepan JJ, Lopes Vaz A, Armas JB, Cannata J, Perez Cano R, Todd C, Khaw KT, da Silva JA, Bhalla A, Poor G, Lyritis G, O'Neill TW, Lunt M, van Duijn CM, de Jong PJ, Breteler MM, Stricker BH, Witteman JC, Compston J, Cooper C, Duncan E, Keen R, McLellan A, Wass J, Cupples LA, Demissie S, Imamovic A, Dekema E, van Essen H, Pluijm S, Deeg D, Mallmin H, Grundberg E, Holmberg A, Orwoll E, Agren A, Sjodin H, Enquist K, Bergdahl I, Bergstrom U (2008) Large-scale analysis of association between LRP5 and LRP6 variants and osteoporosis. JAMA 299: 1277–1290.

99. Langdahl BL, Uitterlinden AG, Ralston SH, **Trikalinos TA**, Balcells S, Brandi ML, Scollen S, Lips P, Lorenc R, Obermayer-Pietsch B, Reid DM, Armas JB, Arp PP, Bassiti A, Bustamante M, Husted LB, Carey AH, Perez Cano R, Dobnig H, Dunning AM, Fahrleitner-Pammer A, Falchetti A, Karczmarewicz E, Kruk M, van Leeuwen JP, Masi L, van Meurs JB, Mangion J, McGuigan FE, Mellibovsky L, Mosekilde L, Nogues X, Pols HA, Reeve J, Renner W, Rivadeneira F, van Schoor NM, Ioannidis JP, Contopoulos-Ioannidis DG, Hugens W, Albagha OM, Macdonald H, Stewart A, Carstens M, Stenkjaer L, Dechairo B, Mackay I, Bennett S, Tanini A, Grinberg D, Diez Perez A, Enjuanes A, Walter D, Hartl U, Gugatschka M, Bonelli C, van Hul W, Parsons C, Bear S, Farmer R, Brixen K, Jensen JE, Eiken P, Lukaszkiewicz J, Bilinski P, Czerwinski E, Lewinski A, Marcinowska-Suchowierska E, Milewicz A, Spaczynski M, Jaworski M, Nuti R, Grazio S, Miazgowski T, Boonen R, Masaryk P, Stepan JJ, Lopes Vaz A, Cannata J, Weber K, Benevolenskaya LI, Todd C, Khaw KT, da Silva J, Bhalla A, Poor G, Bruges Armas J, Lyritis G, O'Neill TW, Lunt M, Compston J, Cooper C, Duncan E, Keen R, McLellan A, Wass J, Dekema E, van Essen H, Pluijm S, Bravenboer N, Hofman A, van Duijn CM, de Jong PJ, Breteler MM, Stricker BH, Witteman JC (2008) Large-scale analysis of association between polymorphisms in the transforming growth factor beta 1 gene (TGFB1) and osteoporosis: the GENOMOS study. Bone 42: 969–981.

100. Ioannidis JP, **Trikalinos TA** (2007) An exploratory test for an excess of significant findings. Clin Trials 4: 245–253.

101. Ioannidis JP, Polyzos NP, **Trikalinos TA** (2007) Selective discussion and transparency in microarray research findings for cancer outcomes. Eur J Cancer 43: 1999–2010.

102. Ioannidis JP, **Trikalinos TA** (2007) The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. CMAJ 176: 1091–1096.

103. Stefanis NC, **Trikalinos TA**, Avramopoulos D, Smyrnis N, Evdokimidis I, Ntzani EE, Ioannidis JP, Stefanis CN (2007) Impact of schizophrenia candidate genes on schizotypy and cognitive endophenotypes at the population level. Biol Psychiatry 62: 784–792.

104. Lathyris DN, **Trikalinos TA**, Ioannidis JP (2007) Evidence from crossover trials: empirical evaluation and comparison against parallel arm trials. Int J Epidemiol 36: 422–430.

105. Pakos EE, **Trikalinos TA**, Fotopoulos AD, Ioannidis JP (2007) Prosthesis infection: diagnosis after total joint arthroplasty with antigranulocyte scintigraphy with 99mTc-labeled monoclonal antibodies–a meta-analysis. Radiology 242: 101–108.

106. Elbaz A, Nelson LM, Payami H, Ioannidis JP, Fiske BK, Annesi G, Carmine Belin A, Factor SA, Ferrarese C, Hadjigeorgiou GM, Higgins DS, Kawakami H, Kruger R, Marder KS, Mayeux RP, Mellick GD, Nutt JG, Ritz B, Samii A, Tanner CM, Van Broeckhoven C, Van Den Eeden SK, Wirdefeldt K, Zabetian CP, Dehem M, Montimurro JS, Southwick A, Myers RM, **Trikalinos TA** (2006) Lack of replication of thirteen single-nucleotide polymorphisms implicated in Parkinson's disease: a large-scale international study. Lancet Neurol 5: 917–923.

107. Ioannidis JP, **Trikalinos TA**, Zintzaras E (2006) Extreme between-study homogeneity in meta-analyses could offer useful insights. J Clin Epidemiol 59: 1023–1032.

108. Evangelou E, **Trikalinos TA**, Salanti G, Ioannidis JP (2006) Family-based versus unrelated case-control designs for genetic associations. PLoS Genet 2: e123.

109. Ioannidis JP, **Trikalinos TA**, Khoury MJ (2006) Implications of small effect sizes of individual genetic variants on the design and interpretation of genetic association studies of complex diseases. Am J Epidemiol 164: 609–614.

110. Salanti G, Higgins JP, **Trikalinos TA**, Ioannidis JP (2007) Bayesian meta-analysis and meta-regression for gene-disease associations and deviations from Hardy-Weinberg equilibrium. Stat Med 26: 553–567.

111. Mantzavinis GD, **Trikalinos TA**, Dimoliatis ID, Ioannidis JP (2006) Self-reported health in high and very high incomes. Qual Life Res 15: 547–558.

112. **Trikalinos TA**, Salanti G, Khoury MJ, Ioannidis JP (2006) Impact of violations and deviations in Hardy-Weinberg equilibrium on postulated gene-disease associations. Am J Epidemiol 163: 300–309.

113. Evangelou E, **Trikalinos TA**, Ioannidis JP (2005) Unavailability of online supplementary scientific information from articles published in major journals. FASEB J 19: 1943–1944.

114. **Trikalinos TA**, Andreadis IA, Asproudis IC (2005) Decision analysis with Markov processes supports early surgery for large-angle infantile esotropia. Am J Ophthalmol 140: 886–893.

115. Pan Z, **Trikalinos TA**, Kavvoura FK, Lau J, Ioannidis JP (2005) Local literature bias in genetic epidemiology: an empirical evaluation of the Chinese literature. PLoS Med 2: e334.

116. Economou M, Manolakopoulos S, **Trikalinos TA**, Filis S, Bethanis S, Tzourmakliotis D, Avgerinos A, Raptis S, Tsianos EV (2005) Interferon-alpha plus lamivudine vs lamivudine reduces breakthroughs, but does not affect sustained response in HBeAg negative chronic hepatitis B. World J Gastroenterol 11: 5882–5887.

117. **Trikalinos TA**, Karvouni A, Zintzaras E, Ylisaukko-oja T, Peltonen L, Jarvela I, Ioannidis JP (2006) A heterogeneity-based genome search meta-analysis for autism-spectrum disorders. Mol Psychiatry 11: 29–36.

118. Pakos EE, Ntzani EE, **Trikalinos TA** (2005) Patellar resurfacing in total knee arthroplasty. A meta-analysis. J Bone Joint Surg Am 87: 1438–1445.

119. Evangelou E, Kyzas PA, **Trikalinos TA** (2005) Comparison of the diagnostic accuracy of lymphatic endothelium markers: Bayesian approach. Mod Pathol 18: 1490–1497.

120. Ioannidis JP, **Trikalinos TA** (2005) Early extreme contradictory estimates may appear in published research: the Proteus phenomenon in molecular genetics research and randomized trials. J Clin Epidemiol 58: 543–549.

121. Contopoulos-Ioannidis DG, Gilbody SM, **Trikalinos TA**, Churchill R, Wahlbeck K, Ioannidis JP (2005) Comparison of large versus smaller randomized trials for mental health-related interventions. Am J Psychiatry 162: 578–584.

122. **Trikalinos TA**, Churchill R, Ferri M, Leucht S, Tuunainen A, Wahlbeck K, Ioannidis JP (2004) Effect sizes in cumulative meta-analyses of mental health randomized trials evolved over time. J Clin Epidemiol 57: 1124–1130.

123. Panidou ET, **Trikalinos TA**, Ioannidis JP (2004) Limited benefit of antiretroviral resistance testing in treatment-experienced patients: a meta-analysis. AIDS 18: 2153–2161.

124. Economou M, **Trikalinos TA**, Loizou KT, Tsianos EV, Ioannidis JP (2004) Differential effects of NOD2 variants on Crohn's disease risk and phenotype in diverse populations: a metaanalysis. Am J Gastroenterol 99: 2393–2404.

125. Ioannidis JP, Ntzani EE, **Trikalinos TA** (2004) 'Racial' differences in genetic effects for complex diseases. Nat Genet 36: 1312–1318.

126. **Trikalinos TA**, Ntzani EE, Contopoulos-Ioannidis DG, Ioannidis JP (2004) Establishment of genetic associations for complex diseases is independent of early study findings. Eur J Hum Genet 12: 762–769.

127. Karassa FB, **Trikalinos TA**, Ioannidis JP (2004) The role of FcgammaRIIA and IIIA polymorphisms in autoimmune diseases. Biomed Pharmacother 58: 286–291.

128. Ziavra N, Kastanioudakis I, **Trikalinos TA**, Skevas A, Ioannidis JP (2004) Diagnosis of sensorineural hearing loss with neural networks versus logistic regression modeling of distortion product otoacoustic emissions. Audiol Neurootol 9: 81–87.

129. Ioannidis JP, **Trikalinos TA**, Law M, Carr A (2003) HIV lipodystrophy case definition using artificial neural network modelling. Antivir Ther (Lond) 8: 435–441.

130. Karassa FB, **Trikalinos TA**, Ioannidis JP (2003) The Fc gamma RIIIA-F158 allele is a risk factor for the development of lupus nephritis: a meta-analysis. Kidney Int 63: 1475–1482.

131. Ioannidis JP, **Trikalinos TA**, Ntzani EE, Contopoulos-Ioannidis DG (2003) Genetic associations in large versus small studies: an empirical assessment. Lancet 361: 567–571.

132. Ioannidis JP, Stavrou I, **Trikalinos TA**, Zois C, Brandi ML, Gennari L, Albagha O, Ralston SH, Tsatsoulis A (2002) Association of polymorphisms of the estrogen receptor alpha gene with bone mineral density and fracture risk in women: a meta-analysis. J Bone Miner Res 17: 2048–2060.

133. Karassa FB, **Trikalinos TA**, Ioannidis JP (2002) Role of the Fcgamma receptor IIa polymorphism in susceptibility to systemic lupus erythematosus and lupus nephritis: a meta-analysis. Arthritis Rheum 46: 1563–1571.

134. Ioannidis JP, **Trikalinos TA**, Danias PG (2002) Electrocardiogram-gated single-photon emission computed tomography versus cardiac magnetic resonance imaging for the assessment of left ventricular volumes and ejection fraction: a meta-analysis. J Am Coll Cardiol 39: 2059–2068.

135. Glantzounis GK, Tselepis AD, Tambaki AP, **Trikalinos TA**, Manataki AD, Galaris DA, Tsimoyiannis EC, Kappas AM (2001) Laparoscopic surgery-induced changes in oxidative stress markers in human plasma. Surg Endosc 15: 1315–1319.

136. **Trikalinos TA**, Ioannidis JP (2001) Discontinuation of *Pneumocystis carinii* prophylaxis in patients infected with human immunodeficiency virus: a meta-analysis and decision analysis. Clin Infect Dis 33: 1901–1909.

137. Ioannidis JP, Ntzani EE, **Trikalinos TA**, Contopoulos-Ioannidis DG (2001) Replication validity of genetic association studies. Nat Genet 29: 306–309.

138. **Trikalinos TA**, Ioannidis JP (2001) Predictive modeling and heterogeneity of baseline risk in meta-analysis of individual patient data. J Clin Epidemiol 54: 245–252.

Refereed Reports, White Papers & Technology Assessments

Agency for Healthcare Research and Quality (AHRQ) Evidence Reports, Comparative Effectiveness Reviews, Technology Assessments and Methods Reports are rigorously peer-reviewed (typically by $5-15$ *referees, contrary to just* $2-4$ *for Journal publications), and are also subjected to open public review. These products carry substantial weight. They are often commissioned to inform national committees and healthcare coverage decisions.*

Some of my Journal publications are based on work performed in herein listed reports; any such papers are listed in the Refereed Journal Articles *section. These are not duplicate publications, and are not considered as such neither by AHRQ nor by the respective journal editors.*

139. **Trikalinos TA**, Adam GP, Jap J, Senturk B, Springs S, Sanders-Schmidler G, Lallinger K, Butler M, Brassure M, Banez L, Berliner E, Gozu A, Balk EM (2019) Web interactive presentation of epc reports: A foray into interactive reports. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

140. Balk EM, Adam GP, Kimmel HJ, Rofeberg V, Saeed I, Jeppson P, **Trikalinos TA** (2018) Nonsurgical treatments for urinary incontinence in women: A systematic review update. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

141. Balk EM, Gazula A, Markozannes G, Kimmel HJ, Saldanha I, Resnik LJ, **Trikalinos TA** (2018) Lower limb prostheses: Measurement instruments, comparison of component effects by subgroups, and

long-term outcomes. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

142. Panagiotou OA, Markozannes G, Kowalski R, Gazula A, Di M, Bond DS, Ryder B, Adam GP, **Trikalinos TA** (2018) Short- and long-term outcomes after bariatric surgery in the Medicare population. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

143. Drucker A, Adam GP, Langberg V, Gazula A, Smith B, Moustafa F, Weinstock MW, **Trikalinos TA** (2017) Treatments for primary basal and squamous cell carcinoma of the skin: A systematic review and network meta-analysis. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

144. Balk EM, Ellis AG, Di M, Adam GP, **Trikalinos TA** (2017) Venous thromboembolism prophylaxis in major orthopedic surgery: Systematic review update. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

145. Springs S, Adam GP, Langberg V, Halladay CW, **Trikalinos TA** (2017) Supplemental project to assess the transparency of reporting requirements: Omega-3 fatty acids and cardiovascular disease. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

146. Adam GP, Springs S, Langberg V, Halladay CW, **Trikalinos TA** (2017) Supplemental project to assess the transparency of reporting requirements: Tympanostomy tubes in children with otitis media. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

147. Steele DW, Adam GP, Di M, Halladay CW, Pan I, Coppersmith N, Balk EM, **Trikalinos TA** (2017) Tympanostomy tubes in children with otitis media. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

148. Dahabreh IJ, Chan JA, Earley A, Moorthy D, Avendano EE, **Trikalinos TA**, Balk EM, Wong JB (2017) Modeling and simulation in the context of health technology assessment: Review of existing guidance, future research needs, and validity assessment. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

149. Adam GP, Di M, Cu-Uvin S, W HC, Smith BT, **Trikalinos TA** (2016) Strategies for improving the lives of women aged 40 and above living with HIV/AIDS. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

150. Dahabreh IJ, **Trikalinos TA**, Balk EM, Wong JB (2016) Guidance for the conduct and reporting of modeling and simulation studies in the context of health technology assessment. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

151. Balk EM, G R, Adam GP, Halladay CW, Langberg VN, Azodo IA, **Trikalinos TA** (2016) Renal artery stenosis management strategies: An updated comparative effectiveness review. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

152. Dahabreh IJ, Adam GP, Halladay CW, Steele DW, Daiello LA, Wieland LS, Zgodic A, Smith BT, Herliczek TW, Shah N, **Trikalinos TA** (2015) Diagnosis of right lower quadrant pain and suspected acute appendicitis. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

153. **Trikalinos TA**, Wieland LS, Adam GP, Zgodic A, Ntzani EE (2014) Decision aids for cancer screening and treatment. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

154. Dahabreh IJ, Steele DW, Shah N, **Trikalinos TA** (2014) Oral mechanical bowel preparation for colorectal surgery. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

155. Dahabreh IJ, Wieland LS, Adam GP, Halladay CW, Lau J, **Trikalinos TA** (2014) Core needle and open surgical biopsy for diagnosis of breast lesions: An update to the 2009 report. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

156. Balk EM, Earley A, Hadar N, Shah N, **Trikalinos TA** (2014) Benefits and harms of routine preoperative testing: Comparative effectiveness. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

157. Guise JM, Chang C, Viswanathan M, Glick S, Treadwell J, Umscheid CA, Whitlock E, Fu R, Berliner E, Paynter R, Anderson J, Motu'apuaka P, **Trikalinos TA** (2014) Systematic reviews of complex multicomponent health care interventions. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

158. **Trikalinos TA**, Trow P, Schmid CH (2013) Simulation-based comparison of methods for meta-analysis of proportions and rates. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

159. **Trikalinos TA**, Dahabreh IJ, Wallace BC, Schmid CH, L LJ (2013) Towards a framework for communicating confidence in methodological recommendations for systematic reviews and meta-analyses. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

160. **Trikalinos TA**, Hoaglin DC, Small KM, Schmid CH (2013) Evaluating practices and developing tools for comparative effectiveness reviews of diagnostic test accuracy: Methods for the joint meta-analysis of multiple tests. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

161. Balk EM, Chung M, Hadar N, Patel K, Yu WW, **Trikalinos TA**, Kong Win Chang L (2013) Assessing the accuracy of Google Translate for the purpose of translating non-English language trials for data extraction. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

162. **Trikalinos TA**, Hoaglin DC, Schmid CH (2013) Empirical and simulation-based comparison of univariate and multivariate meta-analysis for binary outcomes. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

163. Balk EM, Earley A, Patel K, **Trikalinos TA**, Dahabreh IJ (2012) Empirical assessment of within-arm correlation imputation in trials of continuous outcomes. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

164. Dahabreh IJ, **Trikalinos TA**, Lau J, Schmid CH (2012) An empirical assessment of bivariate methods for meta-analysis of test accuracy. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

165. **Trikalinos TA**, Balion CM (2012) Options for summarizing medical test performance in the absence of a "gold standard" (Chapter 9). Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

166. **Trikalinos TA**, Kulasingam S, Lawrence WF (2012) Deciding whether to complement a systematic review of medical tests with decision modeling (Chapter 10). Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

167. **Trikalinos TA**, Balion CM, Coleman CI, Griffith L, Santaguida PL, Vandermeer B, Fu R (2012) Meta-analysis of test performance when there is a "gold standard" (Chapter 8). Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

168. Balk EM, Chung M, Hadar N, Patel K, Yu WW, **Trikalinos TA**, Chang LW (2012) Accuracy of data extraction of non-english language trials with Google Translate. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

169. Kane RL, Guise JM, Hartman K, Rothenberg B, **Trikalinos TA**, Wilt T (2012) Presentation of future research needs. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

170. Carey TS, Sanders GD, Viswanathan M, **Trikalinos TA**, Kato E, Chang S (2012) Framework for considering study designs for future research needs. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

171. Dahabreh IJ, Chung M, Kitsios GD, Terasawa T, Raman G, Tatsioni A, Tobar A, Lau J, **Trikalinos TA**, Schmid CH (2012) Comprehensive overview of methods and reporting of meta-analyses of test accuracy. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

172. **Trikalinos TA**, Lee J, Moorthy D, Yu WW, Lau J, Lichtenstein AH, Chung M (2012) Effects of eicosapentanoic acid and docosahexanoic acid on mortality across diverse settings: Systematic review and meta-analysis of randomized trials and prospective cohorts: Nutritional Research Series, vol. 4. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

173. Dahabreh IJ, Chung M, Kitsios GD, Terasawa T, Raman G, Tatsioni A, Tobar A, Lau J, **Trikalinos TA**, Schmid CH (2012) Evaluating practices and developing tools for comparative effectiveness reviews of diagnostic test accuracy: Comprehensive overview of methods and reporting of meta-analyses of test accuracy. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

174. Chung M, Dahabreh IJ, Hadar N, Ratichek SJ, Gaylor JM, **Trikalinos TA**, Lau J (2011) Emerging MRI technologies for imaging musculoskeletal disorders under loading stress [Internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

175. **Trikalinos TA**, Moorthy D, Chung M, Yu WW, Lee J, Lichtenstein AH, Lau J (2011) Comparison of translational patterns in two nutrient-disease associations: Nutritional Research Series, vol. 5. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

176. **Trikalinos TA**, Dahabreh IJ, Lee J, Moorthy D (2011) Defining an optimal format for presenting research needs [Internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

177. **Trikalinos TA**, Terasawa T, Raman G, Ip S, Lau J (2010) A systematic review of loss-of-heterozygosity based topographic genotyping with PathfinderTG®. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

178. Raman G, Wallace BC, Chung M, Mahoney A, **Trikalinos TA**, Lau J (2010) Update on genetic tests for non-cancer diseases/conditions: A horizon scan. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

179. Raman G, Wallace BC, Patel K, Lau J, **Trikalinos TA** (2010) Update of horizon scans of genetic tests currently available for clinical use in cancers. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

180. Terasawa T, Dahabreh IJ, Castaldi PJ, **Trikalinos TA** (2010) Systematic reviews on selected pharmacogenetic tests for cancer treatment: CYP2D6 for tamoxifen in breast cancer, KRAS for anti-EGFR antibodies in colorectal cancer, and BCR-ABL1 for tyrosine kinase inhibitors in chronic myeloid leukemia. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

181. Fu R, Gartlehner G, Grant M, Shamliyan T, Sedrakyan A, Wilt TJ, Griffith L, Oremus M, Raina P, Ismaila A, Santaguida P, Lau J, **Trikalinos TA** (2010) Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

182. **Trikalinos TA**, Dahabreh IJ, Wong JB, Rao M (2010) Future research needs for the comparison of percutaneous coronary interventions with bypass graft surgery in nonacute coronary artery disease: Identification of future research needs from comparative effectiveness review no. 9 [internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

183. **Trikalinos TA**, Siebert U, Lau J (2009) Decision-analytic modeling to evaluate benefits and harms of medical tests – uses and limitations: Medical Tests White Paper Series [Internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

184. **Trikalinos TA**, Terasawa T, Ip S, Raman G, Lau J (2009) Particle beam radiation therapies for cancer [Internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

185. Chung M, Balk EM, Brendel M, Ip S, Lau J, Lee J, Lichtenstein A, Patel K, Raman G, Tatsioni A, Terasawa T, **Trikalinos TA** (2009) Vitamin D and calcium: A systematic review of health outcomes. Evid Rep Technol Assess (Full Rep) : 1–420.

186. Chung M, Balk EM, Ip S, Raman G, Yu WW, **Trikalinos TA**, Lichtenstein AH, Yetley EA, Lau J (2009) Reporting of systematic reviews of micronutrients and health: A critical appraisal: Nutrition

Research Series, vol. 3. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

187. Russell R, Chung M, Balk EM, Atkinson S, Giovannucci EL, Ip S, Taylor Mayne S, Raman G, Ross AC, **Trikalinos TA**, West KP, Lau J (2009) Issues and challenges in conducting systematic reviews to support development of nutrient reference values: Workshop summary: Nutrition Research Series, vol. 2. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

188. Ip S, Chung M, **Trikalinos TA**, DeVine D, Lau J (2008) Screening for bilirubin encephalopathy [Internet]. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

189. Chung M, Ip S, Yu WW, Raman G, **Trikalinos TA**, DeVine D, Lau J (2008) Interventions in primary care to promote breastfeeding: A systematic review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US) .

190. Lau J, Balk EM, Chung M, DeVine D, Ip S, Raman G, **Trikalinos TA**, Lichtenstein AH (2008) Issues and challenges in conducting systematic reviews to support development of nutrient reference values: Workshop summary. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

191. Balk E, Raman G, Chung M, Cepeda S, **Trikalinos TA**, Chew PW, Krishnamani R (2008) Evaluation of the evidence on benefits and harms of pulmonary artery catheter use in critical care settings. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

192. **Trikalinos TA**, Lau J (2008) Home diagnosis of obstructive sleep apnea-hypopnea syndrome: Modeling diagnostic strategies. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

193. Balk EM, Cepeda S, Ip S, **Trikalinos TA**, O'Donnell T (2008) Horizon scan of invasive interventions for lower extremity peripheral artery disease and systematic review of studies comparing stent placement to other interventions. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

194. Raman G, **Trikalinos TA**, Zintzaras E, Kitsios G, Ziogas D, Ip S, Lau J (2008) Reviews of selected pharmacogenetic tests for non-cancer and cancer conditions. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

195. Balk E, Teplinsky E, **Trikalinos TA**, Chew PW, Chung M, Pittas A (2007) Applicability of the evidence regarding intensive glycemic control and self-monitored blood glucose to medicare patients with type 2 diabetes. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

196. Raman G, Chew PW, **Trikalinos TA**, Teplinsky E, DeVine D, Demmer LA, Lau J (2007) Genetic tests for non-cancer diseases/conditions: A horizon scan. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

197. Bonis PA, **Trikalinos TA**, Chung M, Chew P, Ip S, DeVine DA, Lau J (2007) Hereditary nonpolyposis colorectal cancer: Diagnostic strategies and their implications. Evid Rep Technol Assess (Full Rep) : 1–180.

198. Ip S, Chung M, Raman G, Chew P, Magula N, DeVine D, **Trikalinos TA**, Lau J (2007) Breastfeeding and maternal and infant health outcomes in developed countries. Evid Rep Technol Assess (Full Rep) : 1–186.

199. **Trikalinos TA**, Ip S, Raman G, Cepeda S, Balk EM, D'Ambrosio C, Lau J (2007) Home diagnosis of obstructive sleep apnea-hypopnea syndrome. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

200. **Trikalinos TA**, Raman G, Kupelnick B, Chew PW, Lau J (2006) Pulmonary rehabilitation for COPD and other lung disease. Technical report, Rockville (MD): Agency for Healthcare Research and Quality (US).

Refereed Contributions in Computer Science

In computer science, peer-reviewed Conferences *rather than* Journals *are the most prestigious venue of academic communication. Acceptance to a conference is on the basis of a full* 6 *to* 12*-page paper, which is reviewed by* $2-4$ *referees. Conferences such as* ICML [**?**] *and* KDD [**?**] *are among the most prestigious (comparable to a* JAMA *or* The Lancet *article in the medical world).*

201. Small K, Wallace BC, Brodley CE, **Trikalinos TA** (2011) The constrained weight space SVM: Learning with labeled features. In: International Conference on Machine Learning. ICML '11.

202. Wallace BC, Small K, Brodley CE, **Trikalinos TA** (2010) Active learning for biomedical citation screening. In: Proceedings of the 16th ACM SIGKDD international conference on Knowledge discovery and data mining. New York, NY, USA: ACM, KDD '10, pp. 173–182. doi:10.1145/1835804.1835829.

203. Lease M, Comack GV, Nguyen AT, **Trikalinos TA**, Wallace BC (2016) Systematic Review is e-Discovery in doctors' clothing. In: Medical Information Retrieval Workshop. MedIR 16.

204. Wallace BC, Dahabreh IJ, **Trikalinos TA**, Laws MB, Wilson IB, Charniak E (2014) Identifying differences in physician communication styles with a log-linear transition component model. In: AAAI. pp. 1314–1320.

205. Wallace BC, **Trikalinos TA**, Laws MB, Wilson IB, Charniak E (2013) A generative joint, additive, sequential model of topics and speech acts in patient-doctor communication. In: Empirical Methods in Natural Language Processing. EMNLP '13.

206. Wallace BC, Small K, Brodley CE, Lau J, **Trikalinos TA** (2012) Deploying an interactive machine learning system in an evidence-based practice center: abstrackr. In: Proceedings of the 2nd ACM SIGHIT International Health Informatics Symposium. New York, NY, USA: ACM, IHI '12, pp. 819–824. doi:10.1145/2110363.2110464.

207. Wallace BC, Dahabreh IJ, Moran KH, Brodley CE, **Trikalinos TA** (2013) Active literature discovery for scoping evidence reviews: How many needles are there? In: KDD Workshop on Data Mining for Healthcare. KDD-DMH '13.

208. Wallace BC, Small K, Brodley CE, **Trikalinos TA** (2011) Class imbalance, redux. In: IEEE 11th International Conference on Data Mining (ICDM). IEEE, pp. 754–763.

209. Wallace BC, Small K, Brodley CE, **Trikalinos TA** (2011) Who should label what? Instance allocation in multiple expert active learning. In: SIAM International Conference on Data Mining (SDM). pp. 176-187.

210. Wallace BC, Small K, Brodley CE, Lau J, **Trikalinos TA** (2010) Modeling annotation time to reduce workload in comparative effectiveness reviews. In: Proceedings of the 1st ACM International Health Informatics Symposium. New York, NY, USA: ACM, IHI '10, pp. 28–35. doi:10.1145/1882992.1882999.

Refereed Contributions in Ecology and Evolutionary Biology

211. Wallace BC, Lajeunesse MJ, Dietz G, Dahabreh IJ, **Trikalinos TA**, Schmid CH, Gurevitch J (2017) OpenMEE: Intuitive, open-source software for meta-analysis in ecology and evolutionary biology. Methods in Ecology and Evolution 8: 941–947.

Editorials, Commentaries & Non-refereed Journal Articles

*Some of the herein listed commentaries have been peer reviewed (*see [**?**, **?**, **?**, **?**]*).*

1. Leslie LK, Alexander ME, **Trikalinos TA**, Cohen JT, Parsons SK, Newburger JW (2008) Reexamining the emperor's new clothes: ambiguities in current cardiac screening recommendations for youth with attention deficit hyperactivity disorder. Circ Cardiovasc Qual Outcomes 1: 134–137.

2. Kent DM, **Trikalinos TA** (2009) Therapeutic innovations, diminishing returns, and control rate preservation. JAMA 302: 2254–2256.

3. Li T, Puhan MA, Vedula SS, Singh S, Dickersin K, Cameron C, Dickersin K, Goodman SN, Ad Hoc Network Meta-analysis Methods Meeting Working Group [including Trikalinos, T A] (2011) Network meta-analysis-highly attractive but more methodological research is needed. BMC Med 9: 79.

4. Panagiotou OA, **Trikalinos TA** (2015) Commentary: On Effect Measures, Heterogeneity, and the Laws of Nature. Epidemiology 26: 710–713.

5. Cambra K, **Trikalinos TA**, O'Gara-Kurtis E (2013) The Sum is Greater than its Parts: The Center for Evidence-Based Medicine. R I Med J (2013) 96: 25–26.

6. Rao M, Peter I, **Trikalinos TA** (2010) A lesson from the Zuni Indians: heritability in perspective. Am J Kidney Dis 56: 251–254.

7. **Trikalinos TA** (2010) Nomogram can help estimate risk of serious hyperbilirubinemia in healthy infants. J Pediatr 156: 508–509.

8. Kent DM, **Trikalinos TA**, Hill MD (2009) Are unadjusted analyses of clinical trials inappropriately biased toward the null? Stroke 40: 672–673.

Correspondence

9. Drucker AM, Adam GP, Rofeberg V, Gazula A, Smith B, Moustafa F, Weinstock MA, **Trikalinos TA** (2019) Treatments for primary squamous cell carcinoma and squamous cell carcinoma *in situ* of the skin: a systematic review and network meta-analysis Summary of an Agency for Healthcare Research and Quality Comparative Effectiveness Review. J Am Acad Dermatol (Epub ahead of print).

10. Dahabreh IJ, Kitsios GD, **Trikalinos TA**, Kent DM (2011) The complexity of ABO in coronary heart disease. Lancet 377: 1493–1494.

11. Trikalinos NA, **Trikalinos TA** (2009) Inconsistencies in a study of rifampicin-miconazole-impregnated catheters versus standard catheters. Clin Infect Dis 48: 841–842.

12. Kent DM, **Trikalinos TA**, Thaler DE (2008) Patent foramen ovale and cryptogenic stroke. N Engl J Med 358: 1519–1520.

13. **Trikalinos TA**, Panidou ET, Ioannidis JP (2005) Reply to Badri et al. on 'Limited benefit of antiretroviral resistance testing in treatment-experienced patients: a meta-analysis'. AIDS 19: 1336–1337.

14. **Trikalinos TA**, Karassa FB, Ioannidis JP (2001) Meta-analysis of the association between low-affinity Fcgamma receptor gene polymorphisms and hematologic and autoimmune disease. Blood 98: 1634–1635.

Invited Talks

International

Non-exhaustive list

1. **Trikalinos TA** Decision making with comparative modeling: Application in prostate cancer screening. International Society for Clinical Biostatistics Annual Meeting, Birmingham, UK 8/23/2016.

2. **Trikalinos TA** Decision making under alternative interpretations of the evidence. Application in prostate cancer screening. Grand Rounds, Toronto Health Technology Assessement Group, University of Toronto, Canada 3/18/2016.

3. **Trikalinos TA** A Primer on the Meta-analysis of Medical Test Accuracy. Department for Evidence-based Medicine and Clinical Epidemiology, Danube University Krems, Austria 12/18/2014.

4. **Trikalinos TA** Multidimensional scaling and combinatorial methods for meta-analysis. University of Ottawa, Ottawa, Ontario, Canada 12/05/2011.

5. **Trikalinos TA** Modernizing the systematic review pipeline. University of Ottawa, Ottawa, Ontario, Canada 12/06/2011.

6. **Trikalinos TA** Genetic meta-analysis. 3rd course in Statistical Genetic Analysis of Complex Phenotypes, Bertinoro di Romagna, Italy 06/24-27/2007.

7. **Trikalinos TA** Investigating sufficiency of evidence using recursive cumulative meta-analysis. Conference on Sources of Heterogeneity in Meta-analysis of Randomized Clinical Trials, Bremen, Germany 02/10/2007.

National

Non-exhaustive list

8. **Trikalinos TA** Semiautomation of literature identification for systematic reviews. Evidence-based Practice Centers Methods Webinar 2/11/2020.

9. **Trikalinos TA** Emulation of computationally expensive mathematical models. Institute for Technology Assessment, Massachusetts General Hospital, Boston, MA 11/7/2019.

10. **Trikalinos TA** Evidence synthesis for decision making. Global Clinical Scholars Research Training Program, Harvard University, Cambridge, MA 11/7/2019.

11. **Trikalinos TA** Introduction to evidence based medicine. Global Clinical Scholars Research Training Program, Harvard University, Cambridge, MA 6/1/2019.

12. **Trikalinos TA**, Panagiotou O Health outcomes after bariatric surgical therapies in the medicare population: A technology assessment. Centers for Medicare and Medicaid Services Coverage Advisory Committee Meeting, Baltimore, MD 08/15/2017.

13. **Trikalinos TA** Introduction to evidence based medicine. Global Clinical Scholars Research Training Program, Harvard University, Cambridge, MA 6/6/2017.

14. **Trikalinos TA** Evidence synthesis for decision and policy making. Plenary session, Mini-Symposium in Health, Center for Information and Systems Engineering, College of Engineering, Boston University, Boston, MA 04/07/2017.

15. **Trikalinos TA** Evaluation of diagnostics and introduction to medical decision making. Grand Rounds, Department of Emergency Medicine, Rhode Island Hospital, Providence, RI 02/08/2017.

16. **Trikalinos TA** A gentle primer in network meta-analysis for dermatologists. Department of Dermatology, Rhode Island Hospital, Providence, RI 10/20/2016.

17. **Trikalinos TA** A robust approach to designing cancer screening strategies. Data Science Initiative, Brown University, Providence, RI 10/07/2016.

18. **Trikalinos TA** Designing personalized optimal screening strategies via mathematical optimization. Cancer Intervention and Surveillance Modeling Network semiannual meeting, Baltimore, MD 10/28/2016.

19. **Trikalinos TA** Introduction to evidence based medicine. Global Clinical Scholars Research Training Program, Harvard University, Cambridge, MA 6/3/2016.

20. **Trikalinos TA** Robust optimization approaches to designing optimal screening strategies. Cancer Intervention and Surveillance Modeling Network semiannual meeting, Boston, US 5/11/2016.

21. **Trikalinos TA** Evidence synthesis for diagnostic tests with imperfect reference stadards and ordered performance. Prevention Modeling Lab, TH Chan Harvard School of Public Health, Boston, US 5/6/2016.

22. **Trikalinos TA** A gentle primer in network meta-analysis for pediatricians. Grand Rounds, Department of Pediatrics, Rhode Island Hospital, Providence, RI 4/8/2016.

23. **Trikalinos TA** Evidence synthesis for informing public health decision making. Centers for Disease Control and Prevention, Atlanta, GA 8/19/2015.

24. **Trikalinos TA** An overview of evidence-based methods for assessing comparative effectiveness and safety of interventions. Department of Obstetrics and Gynecology, Women and Infants Hospital, Providence, RI 1/21/2015.

25. **Trikalinos TA** Introduction to evidence based medicine. Global Clinical Scholars Research Training Program, Harvard University, Cambridge, MA 6/3/2015.

26. **Trikalinos TA** Dietary supplements: Is there a recommended approach for evaluating the evidence? American Society of Nutrition, Santa Monica, CA 12/4/2015.

27. **Trikalinos TA** Modernizing evidence synthesis for comparative effectiveness research. Brown Pulmonary Research Conference, Rhode Island Hospital 4/15/2015.

28. **Trikalinos TA** Modernizing Technology Assessments in Healthcare. Meaningful Use of Complex Medical Data (MUCMD) Meeting, The Saban Research Institute, Children's Hospital of Los Angeles 09/08/2014.

29. **Trikalinos TA** Optimizing healthcare decisions with Evidence-based Medicine. Rhode Island Innovation Showcase, Brown University Technology Ventures office 05/06/2014.

30. **Trikalinos TA** Some introduction to CEBM at Brown U, and to network meta-analysis. Department of Psychiatry and Human Behavior, Brown University 01/27/2014.

31. **Trikalinos TA** Decision support tools (decision aids) for early cancer treatment and screening decisions. Process of Care Research Branch, National Cancer Institute 01/27/2014.

32. **Trikalinos TA** The problem of capturing and reusing previous effort in technology assessment in healthcare. Department of Computer Science, Brown University 11/13/2013.

33. **Trikalinos TA** Intro to meta-analysis of complex data – Bayesian network meta-analysis for unordered categorical outcomes with incomplete data. Biostatistics Branch, National Cancer Institute 11/06/2013.

34. **Trikalinos TA** Evidence-based Medicine, the Clinical Data Deluge, and Machine Learning. Industrial Partners Program (IPP) Symposium on Putting Big Data to Work, Brown University 04/25/2013.

35. **Trikalinos TA** Bayesian network meta-analysis for unordered categorical outcomes with incomplete data. 11th American Statistical Association Connecticut Chapter Mini-Conference 03/27/2013.

36. **Trikalinos TA** An overview of methods for evaluating the comparative effectiveness and safety of interventions. Department of Obstetrics and Gynecology, Brown University (Women and Infants Hospital) 01/09/2013.

37. **Trikalinos TA** Do this, not that. Saving money by following medical evidence. The Paul Levinger Professorship Pro Tem Lecture in the Economics of Healthcare, Warren Alpert School of Medicine, Brown University 10/25/2012.

38. **Trikalinos TA** Making sense of data on multiple treatments: A gentle introduction to network meta-analysis. Brown University Center for Alcohol and Addiction Studies Rounds 11/02/2012.

39. **Trikalinos TA** Machine learning and multidimensional visualization applications in Comparative Effectiveness Research. Annual Data and Value Strategy Meeting, Center for Evaluation of Value and Risk in Health, Boston, MA 24/04/2012.

40. **Trikalinos TA** Modernizing knowledge synthesis and integration for comparative effectiveness. Annual Data and Value Strategy Meeting, Center for Evaluation of Value and Risk in Health, Boston, MA 14/04/2011.

41. **Trikalinos TA** Can pharmacogenetics deliver on personalized healthcare? Lessons learned. ACRT/SCTS Joint Annual Meeting, Clinical and Translational Research and Education Meeting , Washington DC 04/2011.

42. **Trikalinos TA** Meta-analysis of diagnostic tests. FDA Public Workshop 'Study Methodology for Diagnostics in the Post-Market Setting' 05/12/2010.

43. **Trikalinos TA** Network meta-analysis methods – software. Johns Hopkins University, Baltimore, MD 05/19/2010.

44. **Trikalinos TA** Network meta-analysis methods – presentation of data. Johns Hopkins University, Baltimore, MD 05/20/2010.

45. **Trikalinos TA** Systematic reviews on selected pharmacogenetic tests for cancer treatment: CYP2D6 for tamoxifen in breast cancer; KRAS for anti-EGFR antibodies in colorectal cancer; BCR-ABL1 for tyrosine kinase inhibitors in CML. Centers for Medicare and Medicaid Services Coverage Advisory Committee Meeting, Baltimore, MD 01/27/2010.

46. **Trikalinos TA** Exploring and explaining between-study heterogeneity in meta-analysis. Academy Health Annual Research Meeting, Boston, MA 06/27/2010.

47. **Trikalinos TA** Empirical insights from genetic meta-analysis: Challenges, biases, and unique considerations. SAMSI (Statistical and Applied Mathematical Sciences Institute) Summer 2008 Program on Meta-analysis: Synthesis and Appraisal of Multiple Sources of Empirical Evidence 06/05/2008.

48. **Trikalinos TA** Obstructive sleep apnea: Modeling different diagnostic strategies. Centers for Medicare and Medicaid Services (CMS) Evidence Forum, Baltimore, MD 08/01/2007.

49. **Trikalinos TA** Home diagnosis of obstructive sleep apnea-hypopnea syndrome. Centers for Medicare and Medicaid Services (CMS) Evidence Forum, Baltimore, MD 01/03/2007.

50. **Trikalinos TA** Pulmonary rehabilitation for chronic obstructive pulmonary disease. Centers for Medicare and Medicaid Services (CMS) Evidence Forum, Baltimore, MD 12/06/2006.

51. **Trikalinos TA** Hereditary nonpolyposis colorectal cancer: Accuracy of diagnostic strategies and implications to patients with colorectal cancer and their families. Centers for Disease Control, Atlanta, GA 09/01/2006.

52. **Trikalinos TA** Methodological challenges in large scale genomics. 26th European Workshop for Rheumatology Research, EWRR, Crete, Greece 02/24/2006.

53. **Trikalinos TA** Secrets and pitfalls of meta-analysis. Greek Society of Applied Medical Education, Athens, Greece 10/2005.

54. **Trikalinos TA** Primer on randomized clinical trials. Orthopaedic Sports Medicine Center of Ioannina, Ioannina, Greece 07/2004.

55. **Trikalinos TA** Temporal evolution of effect sizes in mental health interventions. Psychiatric Clinic, University Hospital, Ioannina, Greece 07/2003.

56. **Trikalinos TA** Assessing oxidative stress intensity in biological fluids. Oxidative DNA damage and isoprostanoid formation. Round Table, 2nd Hellenic conference of free radicals and oxidative stress, Thessaloniki, Greece 10/2000.

Other Exhibitions and Performances

Selected Conference Abstracts - Presented by TA Trikalinos

Non-exhaustive list

57. **Trikalinos TA**, Wallace BC, Jap J, Senturk B, Adam GP, Smith B, Schmid CH, Balk EM, Forbes SP (10/21/2019) Large scale empirical evaluation of machine learning for semi-automating citation screening in systematic reviews. In: 41st Society for Medical Decision Making Annual Meeting, Portland, OR, US. p. Oral Presentation.

58. **Trikalinos TA**, Ellis AG, Iskandar R, Wong JB, Schmid CH (9/23/2019) Active learning designs for emulators of computationally expensive mathematical models in health. In: 14th Annual Meeting of the Society for Research Synthesis Methodology, Chicago, IL, US. p. Oral Presentation.

59. **Trikalinos TA**, Silberholz JM, Bertsimas D (01/11/2018) Optimal healthcare decision making under multiple mathematical models - Application in prostate cancer screening. In: 12th International Conference for Health Policy Statistics, Charleston, SC, US. p. Oral Presentation.

60. **Trikalinos TA**, Forbes SP, Willis B, Iskandar R (10/22-25/2017) On a more honest propagation of uncertainty in stochastic mathematical models. In: 39th Society for Medical Decision Making Annual Meeting, Pittsburgh, PA, US. p. Oral Presentation [top rated].

61. Neumann PJ, Sanders-Schmidler G, Basu A, Brock D, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA, Sculpher MJ, **Trikalinos TA**, Siegel JE, Russell LB, Ganiats TG The 2nd panel's recommendations on evidence synthesis for innforming cost-effectiveness analysis. In: 38th Annual Meeting of the Society for Medical Decision Making, Vancouver, Canada. volume 10/24/2016.

62. **Trikalinos TA**, Cheng WC, Schmid CH, Gatsonis C Network meta-analysis of diagnostic tests. In: 2016 Eastern Nother American Region (ENAR) Spring meeting, Austin, TX. volume 05/08/2016.

63. **Trikalinos TA** (11/2015) On estimating optimization model parameters in Public Health and Medicine. In: Institute for Operations Research and the Management Sciences, Philadelphia, PA, US. p. Oral Presentation.

64. **Trikalinos TA**, Cheng W, Gatsonis C, Schmid CH (10/2015) Network meta-analysis of diagnostic accuracy studies. In: International Conference on Health Policy Statistics, Providence, RI, US. p. Poster Presentation.

65. **Trikalinos TA**, Olkin I (10/2014) A new bivariate beta distribution constructed from the Dirichlet distribution. In: Annual Society for Medical Decision Making Meeting 2014, Miami, FL, US. p. Oral Presentation.

66. **Trikalinos TA**, Olkin I, Schmid CH (8/2014) From meta-analysis to decisionmaking: The case of incomplete polytomous outcome data. In: Joint Statistical Meetings 2014, Boston, MA, US. p. Oral Presentation.

67. **Trikalinos TA**, Jansen JP (8/2014) Multivariate network meta-analysis of progression-free survival and overall survival. In: Joint Statistical Meetings 2014, Boston, MA, US. p. Oral Presentation.

68. **Trikalinos TA**, Hoaglin DC, Small KM, Terrin N, Schmid CH (10/2013) Methods for the joint meta-analysis of multiple tests. In: 35th Annual Meeting of the Society for Medical Decision Making, Baltimore, MD, US. p. Oral Presentation.

69. **Trikalinos TA**, Hoaglin DC, Schmid CH (09/2013) Empirical comparison of univariate and multivariate meta-analysis for categorical outcomes. In: 21st Cochrane Colloquium, Quebec City, Quebec, Canada. p. Oral Presentation.

70. Wallace BC, Small KM, Schmid CH, Lau J, Brodley C, **Trikalinos TA** (07/2011) Semi-automating citation screening for facilitating updating of systematic reviews. In: 6th Annual Meeting of the Society for Research Synthesis Methodology, Ottawa, Ontario, Canada. p. Oral Presentation.

71. **Trikalinos TA**, Dahabreh IJ, Wallace BC, Schmid CH, Lau J (07/2011) Framework for transparent guidance on methodology. In: 6th Annual Meeting of the Society for Research Synthesis Methodology, Ottawa, Ontario, Canada. p. Oral Presentation.

72. **Trikalinos TA**, Rebbapragada U, Wallace BC, Schmid CH, Lau J, Brodley C (07/2009) Automated detection of misclassifications during screening of abstracts for systematic reviews. In: 4th Annual Meeting of the Society for Research Synthesis Methodology, Seattle, WA. p. Oral Presentation.

73. Wallace BC, **Trikalinos TA** (10/2009) Semiautomating citation screening for systematic reviews. In: Genetic Applications in Practice and Prevention Network Initiative Meeting, Ann Arbor, MI. p. Poster Presentation.

74. **Trikalinos TA**, Chung M, Raman G, Lau J, Schmid CH (01/17/2008) Data extraction errors in meta-analyses of diagnostic tests. In: 7th International Conference on Health Policy Statistics, Philadelphia, PA. p. Oral Presentation.

75. **Trikalinos TA**, Chung M, Raman G, Lau J, Schmid CH (07/22/2008) Data extraction errors in meta-analyses of diagnostic tests. In: 3rd Annual Meeting of the Society for Research Synthesis Methodology, Corfu, Greece. p. Oral Presentation.

76. **Trikalinos TA**, Olkin I (07/2007) Fixed effects meta-analysis for mutually exclusive categorical outcomes. In: 2nd Annual Meeting of the Society for Research Synthesis Methodology, Evanston, IL. p. Oral Presentation.

77. **Trikalinos TA**, Ntzani E, Ioannidis JP, Contopoulos-Ioannidis DG (10/2-6/2004) Early evidence from meta-analyses of genetic risk factors is unreliable. In: 12th Cochrane Colloquium, Ottawa, Canada. p. Oral Presentation 82.

78. **Trikalinos TA**, Churcill R, Ferri M, Leucht S, Tuunainen A, Wahbeck K, Ioannidis JP (10/26-31/2003) Evolving effect sizes over time in meta-analyses of randomized trials: An empirical assessment of mental health interventions. In: 11th Cochrane Colloquium, Barcelona, Spain. p. Oral Presentation.

Chairmanships in Conferences

Non-exhaustive list, maintained from 2017 onwards

79. **Trikalinos TA** Chair in session: Network meta-analysis. 2017 Joint Statistical Meetings, Baltimore, MD 08/01/2017.

80. **Trikalinos TA** Meeting co-chair. WHO Meeting on the use of mathematical modeling to inform global recommendations 04/27-29/2016.

81. **Trikalinos TA** Prioritization workshop lead facilitator: Prioritization of research needs for women who are older than 40 years and live with HIV. Office for Women's Health, NIH 05/10/2016.

Selected Conference Abstracts - Presented by Coauthors

Presentation [?] received an award for best Podium presentation.

Non-exhaustive list

82. Forbes SP, Iskandar R, **Trikalinos TA** (10/20-23/2019) Deciding how to decide: Evaluating choice functions for test-and-treat decision analyses with partially-identified expected utility. In: 41st Society for Medical Decision Making Annual Meeting, Portland, OR, US. p. Poster Presentation.

83. Ellis AG, Iskandar R, Schmid CH, Wong JB, **Trikalinos TA** (10/14-17/2018) An efficient sequential algorithm for training emulators to a target level of accuracy. In: 40th Society for Medical Decision Making Annual Meeting, Montreal, Canada. p. Poster Presentation.

84. Danilack V, Kimmel H, Phipps M, **Trikalinos TA** (10/14-17/2018) A network meta-analysis of labor induction interventions to inform a decision analysis. In: 40th Society for Medical Decision Making Annual Meeting, Montreal, Canada. p. Oral Presentation.

85. Forbes SB, **Trikalinos TA** (10/14-17/2018) Bounding the implications of non-compliance in randomized trials of orthopedic surgery. In: 40th Society for Medical Decision Making Annual Meeting, Montreal, Canada. p. Poster Presentation [Winner of the SG Pauker Award in Quantitiative Methods and Theoretical Developments].

86. Pinto D, **Trikalinos TA** (10/14-17/2018) Synthesis of evidence on multicomponent interventions: Models and application to perioperative total joint arthroplasty rehabilitation strategies. In: 40th Society for Medical Decision Making Annual Meeting, Montreal, Canada. p. Poster Presentation.

87. Iskandar R, Alarid-Escudero F, **Trikalinos TA** (10/22-25/2017) On simulating multivariate distributions with arbitrary marginal distributions and dependence structures. In: 39th Society for Medical Decision Making Annual Meeting, Pittsburgh, PA, US. p. Oral Presentation.

88. Kim D, **Trikalinos TA**, Wong JB (10/23/2017) Cumulative network meta-analysis and research prioritization: Evolution of treatment effects for stable coronary artery disease. In: 39th Society for Medical Decision Making Annual Meeting, Pittsburgh, PA, US. p. Oral Presentation [top rated].

89. Ellis AG, Iskandar R, **Trikalinos TA** (10/22-25/2017) An active learning algorithm for efficiently developing meta-models, with an application in prostate cancer screening. In: 39th Society for Medical Decision Making Annual Meeting, Pittsburgh, PA, US. p. Poster Presentation [Lee Lusted Award winner].

90. Forbes SP, Iskandar R, **Trikalinos TA** (10/22-25/2017) Bounding the implications of partial identifiability in decision analysis. In: 39th Society for Medical Decision Making Annual Meeting, Pittsburgh, PA, US. p. Poster Presentation [Lee Lusted Award finalist].

91. Adam GP, Springs SL, **Trikalinos TA**, Williams JW, Eaton J, Von Isenburg M, Gierisch JM, Wilson LM, Sharma R, Dy SM, Waldfogel JM, Robinson KA, Viswanathan M, Cook-Middleton J, Forman-Hoffman VL, Berliner E, Kaplan RM Augmenting systematic reviews with information from clinicaltrials.gov to increase transparency and reduce bias. In: Peer Review Congress, Chicago, IL. volume 9/10/2017, p. Oral Presentation.

92. Alarid-Escudero F, Jalal H, **Trikalinos TA** Opportunity cost of non-rigorous or non-transferable research: Implications for economic evaluation. In: 6th Latin American Conference of the International Society of Pharmacoeconomics and Outcomes Research, Sao Paulo, Brazil. volume 9/16/2017, p. Poster Presentation.

93. Iskandar R, **Trikalinos TA** Simulating multivariate distributions with arbitrary marginal distributions and dependence structures. In: 22nd Annual Meeting of the International Society for Pharmacoecomonics and Outcomes Research, Boston, MA. volume 05/20-24/2017, p. Poster Presentation.

94. Ellis AG, Iskandar R, Schmid CH, Wong JB, **Trikalinos TA** An active learning algorithm for efficient development of emulators of complex model, with an application in prostate cancer screening. In: 22nd Annual Meeting of the International Society for Pharmacoecomonics and Outcomes Research, Boston, MA. volume 05/20-24/2017, p. Poster Presentation.

95. Forbes SP, Di M, Salomon JA, Linas BP, **Trikalinos TA** Evidence synthesis for diagnostic tests with partially ordered performance and no reference test. In: 22nd Annual Meeting of the International Society for Pharmacoecomonics and Outcomes Research, Boston, MA. volume 05/20-24/2017, p. Poster Presentation.

96. Drucker A, Adam GP, Langberg V, Gazula A, Smith B, Moustafa F, Weinstock MW, **Trikalinos TA** Treatments for primary basal and squamous cell carcinoma of the skin: A systematic review and network meta-analysis. In: 76th Annual Meeting of the Society for Investigative Dermatology, Portland, OR. volume 04/26-29/2017, p. Oral Presentation.

97. Alarid-Escudero F, Jalal H, **Trikalinos TA** On the opportunity cost of non-rigorous or non-transferable research: Implications for economic evaluation. In: 38th Annual Meeting of the Society for Medical Decision Making, Vancouver, Canada. volume 10/24/2016, p. Oral Presentation.

98. Forbes SP, Di M, Salomon JA, Linas BP, **Trikalinos TA** Evidence synthesis for diagnostic tests with partially ordered performance and no reference standard. In: 38th Annual Meeting of the Society for Medical Decision Making, Vancouver, Canada. volume 10/24/2016, p. Poster Presentation [Lee Lusted Award winner].

99. Linas BP, Tasillo A, Menzies N, Horsburgh RC, Marks SM, **Trikalinos TA**, Salomon JA (5/2016) The cost-effectiveness of testing and treatment for latent tuberculosis infection among foreign-born persons in the U.S. In: American Thoracic Society Meeting, San Fransisco, CA, US. p. Poster Presentation.

100. Forbes S, **Trikalinos TA**, Dahabreh IJ (6/2016) Evidence synthesis using randomized and non-randomized studies of the effects of interventions: Recommendations for practice. In: Academy Health Annual Research Meeting, Boston, MA, US. p. Poster Presentation.

101. Ellis AG, **Trikalinos TA**, Wong JB, Dahabreh IJ (5/2016) An overview of statistical methods for meta-analysis combining individual participant data and aggregate data. In: 21st Annual International

Meeting, International Society For Pharmacoeconomics and Outcomes Research – ISPOR, Washington DC, US. p. Poster Presentation.

102. Forbes S, **Trikalinos TA**, Dahabreh IJ (10/2015) Evidence synthesis using randomized and non-randomized studies of the effects of interventions: Recommendations for practice. In: International Conference on Health Policy Statistics, Providence, RI, US. p. Poster Presentation.

103. Silberholz JM, Bertsimas D, **Trikalinos TA** (11/2015) A robust optimization approach to designing cancer screening strategies. In: Institute for Operations Research and the Management Sciences, Philadelphia, PA, US. p. Oral Presentation.

104. Dahabreh IJ, **Trikalinos TA** (5/2015) Concepts of similarity in evidence synthesis. In: Society for Research Synthesis Methods Annual Meeting, Nashville, TN, US. p. Oral Presentation.

105. Dahabreh IJ, Wong JB, Balk EM, **Trikalinos TA** (5/2015) Guidance for the conduct and reporting of modeling and simulation in the context of health technology assessment. In: 20th Annual International Meeting, International Society For Pharmacoeconomics and Outcomes Research – ISPOR, Philadelphia, PA, US. p. Oral Presentation.

106. Zgodic A, **Trikalinos TA**, Olkin I, Schmid CH, Lau J, Dahabreh IJ (8/2014) Implications of different evidence-summaries for contextualizing and interpreting findings of meta-analysis of diagnostic tests. In: Joint Statistical Meetings 2014, Boston, MA, US. p. Oral Presentation.

107. Jansen JP, **Trikalinos TA** (10/2013) Mmultivariate network meta-analysis of progression-free survival and overall survival. In: 16th Annual European Meeting, International Society For Pharmacoeconomics and Outcomes Research – ISPOR. p. Oral Presentation.

108. Halladay CW, **Trikalinos TA**, Schmid IC, Schmid CH, Dahabreh IJ (10/2013) Searching for studies beyond Pubmed: What is the benefit of searching multiple databases? In: 35th Annual Meeting of the Society for Medical Decision Making, Baltimore, MD, US. p. Poster Presentation.

109. Ivers N, **Trikalinos TA**, Dahabreh IJ, Tricco A, Moher D, Ramsay T, Yu C, Straus S, Grimshaw J (2013) Does hierarchical meta-regression provide key insights for exploring the effectiveness of complex quality improvement interventions in diabetes? In: 21st Cochrane Colloquium, Quebec City, Quebec, Canada.

110. Dahabreh IJ, Terasawa T, Moorthy D, Lamont JL, Chen ML, **Trikalinos TA** (2012) Repurposing randomized controlled trials of therapeutic interventions to identify molecular biomarkers for treatment choice: Case studies in oncology and cardiovascular disease. In: Agency for Healthcare Research and Quality Annual Conference, Washington, DC.

111. Dahabreh IJ, **Trikalinos TA**, Joseph L, Schmid CH (2012) An empirical assessment of bivariate methods for meta-analysis of test performance. In: 20th Cochrane Colloquium, Auckland, New Zealand.

112. Dahabreh IJ, Chung M, Kitsios GD, Raman G, Tatsioni A, Tobar A, Lau J, **Trikalinos TA**, Schmid CH (2012) Comprehensive overview of methods and reporting of meta-analyses of test accuracy. In: 20th Cochrane Colloquium, Auckland, New Zealand.

113. **Trikalinos TA**, Hoaglin DC, Small KM, Schmid CH (2012) Methods for the joint meta-analysis of multiple tests. In: 20th Cochrane Colloquium, Auckland, New Zealand.

114. **Trikalinos TA**, Hoaglin DC, Small K, Schmid CH (2012) Methods for the joint meta-analysis of multiple tests. In: Society for Research Synthesis Methodology Annual Meeting, Provence, France.

115. Alreja G, Chandrasekaran D, **Trikalinos TA**, Rothberg M (2011) Oral anticoagulants for secondary prophylaxis of stroke in coronary artery disease and cerebrovascular accident. In: J Am Coll Cardiol. volume 57 (S1), p. E1509.

116. Golden WM, **Trikalinos TA**, Wong JB (2007) Integrating direct and indirect comparisons of drug efficacy data with meta-analysis. In: Med Decis Making.

117. Schmid CH, **Trikalinos TA**, Olkin I (2007) Random-effects meta-analyses for outcomes with three or more mutually exclusive categorical responses. In: Society for Research Synthesis Methodology Annual Meeting, Chicago, IL.

118. Dahabreh IJ, Kitsios GD, **Trikalinos TA**, Kent DM (2010) Ischemic stroke and coronary artery disease share a common genetic background: An empirical investigation of validated associations. In: Stroke. volume 124, p. E336.

119. Wessler BS, Kramer DG, **Trikalinos TA**, Kent DM, Konstam MA, Udelson JE (2009) Drug and device effects on peak oxygen consumption as a predictor of therapeutic effects on mortality in heart failure randomized trials. In: Circulation. volume 120, p. S733.

120. Economou M, **Trikalinos TA**, Loizou K, Tsianos E, Ioannidis JP (2004) Consistency of the association between NOD2/CARD15 polymorphisms and Crohn's disease susceptibility and phenotype across diverse populations: A meta-analysis. Gastroenterology 126: A358.

121. Wong JB, Wu C, **Trikalinos TA** (2009) Anginal outcomes in initial percutaneous coronary interventions versus medical therapy: A meta-analysis of randomized controlled trials. J Am Coll Cardiol 53: A377.

122. Wallace BC, Schmid CH, Lau J, Brodley C, **Trikalinos TA** (07/2009) Semi-automated screening of biomedical citations for systematic reviews. 4th Annual Meeting of the Society for Research Synthesis Methodology, Seattle, WA : Oral Presentation.

123. Shah AK, Retana AK, **Trikalinos TA**, Wong JB (2008) Stroke in coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI): A meta-analysis of randomized trials. J Am Coll Cardiol 51: A250.

124. Kent DM, **Trikalinos TA** (2007) Are 'treatment' bare metal stents superior to 'control' bare metal stents? A meta-analytic approach. Cardiovasc Drugs Therapy 21: S16.

125. Stefanis NC, **Trikalinos TA**, Avramopoulos D, Smyrnis N, Evdokimidis I, Ntzani EE, Ioannidis JP, Stefanis CN (2007) Impact of schizophrenia candidate genes on schizotypy and cognitive endophenotypes at the population level. Eur Psychiatry 22: S19-S20.

126. Ioannidis JP, **Trikalinos TA**, Danias PG (2002) Does ECG-gated SPECT provide accurate measurement of left ventricular election fraction and volumes? A meta-analysis. J Am Coll Cardiol 39: 394A.

127. Rodday AM, Leslie L, Cohen J, Triedman J, Alexander M, Ip S, Newburger J, Parsons S, **Trikalinos TA**, Wong J (2012) Population screening trade offs: A systematic review and meta-analysis of screening asymptomatic children for cardiac disorders that cause sudden cardiac death. Med Decis Making 32: E98.

128. **Trikalinos TA**, Ioannidis JP (10/2001) Semi-automated screening of biomedical citations for systematic reviews. 8th Cochrane Colloquium, Cape Town, South Africa : Poster Presentation C09.

129. Ioannidis JP, **Trikalinos TA** (10/2004) Early extreme contradictory estimates in published research. 12th Cochrane Colloquium, Ottawa, Ontario, Canada : Oral Presentation 60.

130. **Trikalinos TA**, Ioannidis JP (10/2004) Genetic risk factors for complex diseases: race is not important. 12th Cochrane Colloquium, Ottawa, Ontario, Canada : Oral Presentation 71.

131. Gilbody S, **Trikalinos TA**, R C, Wahbeck K, Ioannidis JP (10/2004) Comparison of large versus smaller randomized trials for mental health-related interventions. 12th Cochrane Colloquium, Ottawa, Ontario, Canada : Poster Presentation 150.

132. Ioannidis JP, **Trikalinos TA** (10/2006) Appropriateness of asymmetry tests for publication bias in meta-analysis: A large scale survey. 14th Cochrane Colloquium, Dublin, Ireland : Oral Presentation 22.

133. Ioannidis JP, **Trikalinos TA** (10/2006) Significance chasing bias: Conceptual framework and an exploratory test. 14th Cochrane Colloquium, Dublin, Ireland : Poster Presentation 149.

134. Ioannidis JP, **Trikalinos TA**, Zintzaras E (10/2006) Extreme between-study homogeneity in meta-analysis. 14th Cochrane Colloquium, Dublin, Ireland : Poster Presentation 150.

135. van Meurs JB, **Trikalinos TA**, Ralston SH, Balcells S, Brandi ML, Brixen K, Kiel DP, Langdahl BL, Lips P, Ljunggren O, Lorenc R, Obermayer-Pietsch B, Ohlsson C, Pettersson U, Reid DM, Rousseau F, Scollen S, van Hul W, Agueda L, Akesson K, Benevolenskaya LI, Ferrari SL, Hallmans G, Hofman A, Husted LB, Kruk M, Kaptoge S, Karasik D, Karlsson MK, Lorentzon M, Masi L, McGuigan FE, Mellström D, Mosekilde L, Nogues X, Pols HA, Reeve J, Renner W, Rivadeneira F, van Schoor NM, Weber K, Ioannidis JP, Uitterlinden AG, GENOMOS Study (09/2007) Large-scale analysis of association between polymorphisms in the LRP-5 and -6 genes and bone mineral density and fracture. In: J Bone Mineral Res. volume 22, p. S56.

Research Grants & Contracts

Organized first by Ongoing *vs.* Completed. *All listed awards are competitive. I do not list peer-reviewed institutional (internal) seed funds. I do not list* Grants and Contracts *that were completed between 2006 and 2012 (when I was at Tufts Medical Center), and before 2006 (when I was in Greece).*
Last updated on Thursday 8th October, 2020.

Ongoing

Type	Grant
Grant	HS027247-01: Semi-automated identification of biomedical literature.
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$100,000
Period	9/30/2019–9/29/2020
Role	Principal Investigator

Type	Grant
Title	K12 HS022998: Develop Patient Centered Outcomes Scholars for Comparative Effectiveness Research
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$3.8 million
Period	8/1/2014–8/31/2020
Role	Principal Investigator

Type	Grant
Grant	R25HS023299-01: Innovative Training to Improve CER PCOR Systematic Review Production and Uptake
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$2.5 million
Period	8/1/2014–8/31/2020
Role	Co-Investigator (Principal Investigator CH Schmid)

Type	Grant
Grant Title	R01LM012086-01A I Semi-Automating Data Extraction for Systematic Reviews
Funder	National Library of Medicine (NLM)
Amount	Subcontract $119,150 (Total $880,629)
Period	1/1/2016- 12/31/2019
Role	Subcontract Principal Investigator (Principal Investigator BC Wallace, Northeastern University)

Type	Grant
Grant	R03HS25840-01A1: Quantifying the Extent of Replicability in Systematic Reviews and Meta-analyses: Implications for Grading of the Strength of Evidence.

Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$61,474
Period	3/1/2019–2/28/2020
Role	Co-Investigator (Principal Investigator O Panagiotou)

The Evidence-based Practice Center (EPC) V Contract is an Indefinite Duration–Indefinite Quantity (IDIQ) Master Contract. It includes several competitive research contracts. I list all contracts under the IDIQ master contact in a section demarcated by '↓ EPC V section' and '↑ EPC V section'. Listing is analogous for sections pertaining to EPC IV and EPC III.

↓ EPC V section

Type	**Indefinite Duration–Indefinite Quantity (IDIQ) Contract**
Title	HHSA290201500002: **Evidence-Based Practice Centers (EPC) V**
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	Total $7 million
Period	9/1/2015–8/31/2019
Role	Principal Investigator

Type	Task Order 11 ⊂ **EPC V** (PI TA Trikalinos)
Title	Topic Refinement & Systematic Review: Interventions for Substance Use Disorders in Adolescents
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$625,000
Period	4/30/2018–8/06/2019 (extension through 01/09/2019)
Role	Co-Investigator (Principal Investigator DW Steele)

Type	Task Order 12 ⊂ **EPC V** (PI TA Trikalinos)
Title	SRDR 2.0 for Digitally Enabling Systematic Review Data
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$1.7 million
Period	4/30/2018–12/11/2020
Role	Co-Investigator (Principal Investigator I Saldanha)

Type	Task Order 13 ⊂ **EPC V** (PI TA Trikalinos)
Title	Management of Acute Diverticulitis
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$480,000
Period	3/29/2019–6/19/2020
Role	Co-Investigator (Principal Investigator EM Balk)

Type	Task Order 14 ⊂ **EPC V** (PI TA Trikalinos)
Title	Management of Primary Headaches in Pregnancy
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$380,000
Period	4/26/2019–8/6/2020
Role	Co-Investigator (Principal Investigator I Saldanha)

Type Task Order 17 ⊂ **EPC V** (PI TA Trikalinos)
Title Management of Obstructive Sleep Apnea in the Medicare Population
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $500,000
Period 9/10/2019–5/3/2021
Role Principal Investigator

Type Task Order 1 ⊂ **EPC V** (PI TA Trikalinos)
Title Methods and Dissemination: Collaboration to improve validity, consistency, and utility of systematic reviews
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $220,000
Period 9/1/2015–8/31/2019
Role Principal Investigator

↑ EPC V section

Completed

Type Contract
Title 5U38PS004644: Prevention Policy Modeling Lab Consortium
Funder Centers for Disease Control and Prevention (CDC)
Amount Subcontract $215,752 (Total $5,875,000)
Period 9/30/2015- 9/29/2019
Role Subcontract Principal Investigator (Principal Investigator J Salomon, Harvard University)

Type Grant
Title U54GM115677: Computational Health Services Research to Identify Use of Low-Value Care in Rhode Island
Funder Advance–Clinical & Translational Research (CTR)/National Institute of General Medical Sciences (NIMGS)
Amount $81,250
Period 5/1/2018–4/30/2019
Role Co-Principal Investigator, with O Panagiotou

Type Grant
Title 1P20GM125507: COBRE Center on Opioids and Overdose
Funder National Institutes of Health (NIH)
Amount $19,713 (Total: $2,555,339)
Period 9/1/2018–1/30/2019
Role Co-Investigator (PI: J Rich)

↓ EPC V section

Type Task Order 10 ⊂ **EPC V** (PI TA Trikalinos)
Title Nonsurgical Treatments for Urinary Incontinence in Adult Women
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $255,000
Period 4/1/2017–6/30/2018
Role Co-Investigator (Principal Investigator EM Balk)

Type Task Order 9 ⊂ **EPC V** (PI TA Trikalinos)
Title Technology Assessment: Bariatric Surgery Interventions
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $200,000
Period 4/1/2017–6/30/2018
Role Principal Investigator

Type Task Order 8 ⊂ **EPC V** (PI TA Trikalinos)
Title Topic Refinement & Systematic Review: Error reduction for Lower Limb Prostheses
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $480,000
Period 6/20/2016 - 6/19/2018
Role Principal Investigator

Type Task Order 7 ⊂ **EPC V** (PI TA Trikalinos)
Title Topic Refinement & Systematic Review: Treatments for Non-Melanoma Skin Cancer
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $355,000
Period 1/26/2016 - 8/1/2017
Role Principal Investigator

Type Task Order 6 ⊂ **EPC V** (PI TA Trikalinos)
Title Strategies for Improving the Lives of Women Age 40 and Above Living with HIV/AIDS
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $200,000
Period 10/16/2015- 5/26/2016
Role Principal Investigator

Type Task Order 5 ⊂ **EPC V** (PI TA Trikalinos)
Title Methods Project: Transparency of Reporting (Ω-3 Fatty Acids Systematic Review)
Funder Agency for Healthcare Research and Quality (AHRQ)
Period 8/19/2015- 12/23/2015
Amount $25,000
Role Co-Investigator (Principal Investigator SL Springs)

Type Task Order 4 ⊂ **EPC V** (PI TA Trikalinos)
Title Methods Project: Transparency of Reporting (Tympanostomy Tubes Systematic Review)
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $25,000
Period 8/19/2015- 5/29/2016

Role Co-Investigator (Principal Investigator GP Adam)

Type Task Order 3 ⊂ **EPC V** (PI TA Trikalinos)
Title Treatment Strategies for Patients with Lower Extremity Peripheral Venous Disease
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $500,000
Period 9/14/2015- 9/4/2016
Role Co-Investigator (Principal Investigator EM Balk)

Type Task Order 2 ⊂ **EPC V** (PI TA Trikalinos)
Title Topic Refinement & Systematic Review: Comparative Effectiveness and Safety of Tympanostomy Tubes in Otitis
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $380,000
Period 2/25/2015- 7/5/2016
Role Principal Investigator

↑ EPC V section

Type Contract
Title Evidence review for a full update of the 2008 Clinical Practice Guideline for the Prevention, Diagnosis, Evaluation and Treatment of Hepatitis C in Chronic Kidney Disease
Funder Kidney Disease – Improving Global Outcomes (KDIGO)
Amount $299,816
Period 9/1/2015- 7/10/2018
Role Co-Investigator (Principal Investigator EM Balk)

Type Grant (site subcontract)
Grant Title DBI-1262442 I Collaborative Research: ABI Development: Making Advanced Statistical Tools Accessible for Quantitative Research Synthesis and Discovery in Ecology and Evolutionary Biology
Funder National Science Foundation (NSF)
Amount $143,124
Period 9/1/2014- 4/30/2016
Role Subcontract Principal Investigator (Principal Investigator BC Wallace)

↓ EPC IV section

Type **Indefinite Duration–Indefinite Quantity (IDIQ) Contract**
Title HHSA290201200012: **Evidence-Based Practice Centers (EPC) IV**
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $4.5 million
Period 08/02/2012–07/31/2017
Role Principal Investigator

Type Task Order 7 ⊂ **EPC IV** (PI TA Trikalinos)

Title Effects of Omega-3 Fatty Acids on Cardiovascular Disease
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $500,000
Period 9/1/2014- 8/31/2015
Role Co-Investigator (Principal Investigator EM Balk)

Type Task Order 6 ⊂ **EPC IV** (PI TA Trikalinos)
Title Updates and Systematic Reviews for the Effective Healthcare Program - Renal Artery Stenosis
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $250,000
Period 5/29/2014- 3/29/2015
Role Co-Investigator (Principal Investigator EM Balk)

Type Task Order 5 ⊂ **EPC IV** (PI TA Trikalinos)
Contract Title Decision Support Tools for Treatment of Pre-malignancies or Early Stage Cancers in Adults
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $225,000
Period 6/24/2013- 5/23/2014
Role Principal Investigator

Type Task Order 4 ⊂ **EPC IV** (PI TA Trikalinos)
Title HHSA 290 2012 00012 I Diagnosis of Acute Appendicitis
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $500,000
Period 6/24/2013- 8/23/2014
Role Co-Investigator (Principal Investigator IJ Dahabreh)

Type Task Order 3 ⊂ **EPC IV** (PI TA Trikalinos)
Title Systematic Review Data Repository: Testing and Maintenance
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $1.8 million
Period 2/1/2013- 1/31/2018
Role Co-Investigator (Principal Investigator EM Balk)

Type Task Order 2 ⊂ **EPC IV** (PI TA Trikalinos)
Contract Title Evidence Synthesis and Translation under MMA Section 1013: Area of Concentration 6
Funder Agency for Healthcare Research and Quality (AHRQ)
Amount $975,000
Period 9/25/2012- 3/25/2014
Role Principal Investigator

Type Task Order 1 ⊂ **EPC IV** (PI TA Trikalinos)
Title Methods and Dissemination: Collaboration to improve validity, consistency, and utility of systematic reviews
Funder Agency for Healthcare Research and Quality (AHRQ)

Amount $294,000
Period 9/1/2012- 8/31/2017
Role Principal Investigator

↑ EPC IV section

Type Contract
Title HHSN261201200390P: Knowledge Integration – Benefit-risk prediction for cancer treatment management
Funder National Cancer Institute (NCI)
Amount $150,000
Period 9/17/2012- 9/16/2013
Role Principal Investigator

Type Contract
Title Integrating causal inference, evidence synthesis and research prioritization methods
Funder Patient Centered Outcomes Research Institute (PCORI)
Amount Subcontract $280,000 (Total $1.1 million)
Period 2012–2015
Role Subcontract Principal Investigator (Principal Investigator JB Wong, Tufts Medical Center)

Type Contract
Title HHSN261201300395P: Treatment Management of Rare Cancers: Understanding and Evaluating Prediction Tools
Funder National Cancer Institute (NCI)
Amount $45,000
Period 9/20/2013- 9/19/2014
Role Co-Investigator (Principal Investigator IJ Dahabreh)

Type Grant
Title Sociolinguistically Informed Natural Language Processing: Automating Irony Detection
Funder Army Research Office (ARO)
Amount $75,678
Period 9/1/2013- 8/31/2015
Role Co-Investigator (Principal Investigator BC Wallace)

Type Grant (Site subcontract)
Grant MOP-1233345: Seeing the forests and the trees - Innovative approaches to exploring heterogeneity in systematic reviews of complex knowledge translation interventions to enhance policy decision making
Funder Canadian Institutes of Health Research (CIHR)
Amount $92,030
Period 10/1/2012- 3/31/2015
Role Subcontract Principal Investigator (Principal Investigator J Grimshaw, Ottawa Hospital Research Institute)

Type Grant
Title R01 HS018494: Semi-automating citation screening for systematic reviews

Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$1.2 million
Period	12/01/2009–11/30/2013
Role	Principal Investigator

Type	Grant
Grant	R01 HS018574: Modernizing Meta-Analysis to Facilitate Comparative Effectiveness Reviews
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	$1.2 million
Period	12/01/2009–11/30/2013
Role	Co-Investigator (Principal Investigator Christopher H. Schmid)

↓ EPC III section

Type	**Indefinite Duration–Indefinite Quantity (IDIQ) Contract**
Title	HHSA290200710055 I: **Evidence-Based Practice Centers (EPC) III**
Funder	Agency for Healthcare Research and Quality (AHRQ)
Amount	Total ∼ $15.3 million
Period	09/01/2007–08/31/2012
Role	Investigator & CoDirector (Principal Investigator & Director J Lau, Tufts Medical Center)

I do not list Task Orders under EPC III (Tufts Medical Center) where I was a co-investigator.

↑ EPC III section

Teaching

Regular Courses

PHP2415 **Introduction to Evidence-based Medicine**, *with J Lau: Spring 2013, Spring 2014; Spring 2015, Fall 2015; with AG Ellis: Spring 2016; Spring 2017, 2018, & 2020.*

PHP2435 **Intermediate Evidence-based Medicine & Meta-analysis**, *Fall 2013.*

PHP2455A **Methods for Health Services and Comparative Effectiveness Research - A**, *Fall 2014.*

PHP2455B **Methods for Health Services and Comparative Effectiveness Research - B**, *Spring 2015.*

PHP2465A **Introduction to Health Decision Science**, *with R Iskandar: Fall 2017; with R Iskandar & SP Forbes: Fall 2018; Fall 2019.*

Seminar or Independent Study Courses

PHP2980 **Graduate Independent Study and Thesis Research (SA5)**, *Spring 2014; Spring 2015; Spring 2016 ($n = 3$); Spring 2017 (n=2).*

PHP2950 **PhD Student Journal Club & Faculty Forum**, *Fall 2013*, student-run course, with minimal faculty oversight.

Guest Lectures in other Courses

CSCI1951A **Introduction to Data Science**, *05/01/2014, 05/03/2016*, 'Data science applications in technology assessment and research synthesis', Course Instructor: Tim Kraska. Department of Computer Science, Brown University.

PHP2180 **Interpretation and Application of Epidemiology**, *03/06/2013*, 'Meta-analysis in Epidemiology', Course Instructor: David Savitz. Department of Epidemiology, Brown University.

PHP2690A **Advanced Topics in Biostatistics**, *Spring 2013*, 'Connections to Research Synthesis, Decision Analysis, Value of Information Analysis', Course Instructor: Christopher Schmid. Department of Biostatistics, Brown University.

Short Courses & Electronic Teaching Modules

No overlap with items in the Invited Talks *section*

2017 **Introduction to Network Meta-analysis**, *Half day course together with Christopher H. Schmid and Valerie Langberg (of Brown University) at the Joint Statistical Meetings (Aug 2017).*

2016 **Introduction to Network Meta-analysis**, *Half day course together with Christopher H. Schmid and Valerie Langberg (of Brown University) at the Joint Statistical Meetings (Aug 2016).*

2015 **Introduction to Evidence-based Medicine**, *Two-day course together with Christopher H. Schmid (of Brown University) at the CDC (17-18 Aug 2015).*

2014 **Introduction to Evidence-based Medicine**, *Two-day course together with Joseph Lau and Christopher H. Schmid (both of Brown University) at the Brown University Warren Alpert Medical School.*

2013 **Advanced meta-analysis**, *Full-day course together with Issa J. Dahabreh (Brown University) at the Society for Medical Decision Making annual meeting.*

2008–2011 **Introduction to meta-analysis**, *Full-day course together with Ingram Olkin (Stanford University) at the Society for Medical Decision Making annual meetings.*

2007–2010 **Introduction to meta-analysis**, *Summer course of the Clinical and Translational Science Program, Sackler School, Tufts University.*

2009–2011 **Methods for quantitative synthesis and primer in advanced meta-analysis**, *Annual Short Course in Comparative Effectiveness Research, Tufts CTSI.*

2011 **Assessing Pharmacogenetic Information in Clinical Trials**, *Comparative Effectiveness Research (CER) Survey Course, Tufts CTSI.*

2010 **Online training module: 'Systematic Review: Data extraction'**, *with J Lau, M McPheeters, and J Seroogy. Part of a selection of 12 recorded training lectures for training researchers who perform systematic reviews..*

2010 **Online training module: 'Systematic Review: Presentation of Findings'**, *with J Lau, and M McPheeters. Part of a selection of 12 recorded training lectures for training researchers who perform systematic reviews..*

2010 **Online training module: 'Systematic Review: Quantitative Synthesis I'**, *with J Lau. Part of a selection of 12 recorded training lectures for training researchers who perform systematic reviews..*

2010 **Online training module: 'Systematic Review: Quantitative Synthesis II'**, *with J Lau. Part of a selection of 12 recorded training lectures for training researchers who perform systematic reviews..*

2007 **Introduction to non-parametric and parametric meta-analysis and hands-on workshop**, *3rd course in Statistical Genetic Analysis of Complex Phenotypes, Bertinoro di Romagna, Italy.*

Mentoring

Students & Fellows Mentored, Honors, Masters & PhD theses

I have been on the advisory committee of the following fellows and students:

Current

Brown University Doctoral students

–Shaun P. Forbes, PhD Candidate in Health Services Research (Thesis advisor)

–Mauricio Lopez-Mendez, PhD Student in Health Services Research (co-Advisor, with R Iskandar)

Past *I have coauthored papers with Wallace, Small, Yu, Kitsios, Dahabreh, Tobar, Gabbay, Kelly, Ellis*

Brown University

Doctoral students

–Wei Cheng, PhD in Biostatistics 2016 (Thesis committee member)
–Alexandra G. Ellis, MS, PhD in Health Services Research 2017 (Thesis advisor)

MS students
–Bo Wang, MS in Biostatistics 2017 (Thesis reader, joint supervision with CH Schmid)
–Yuanfei Chen, MS in Biostatistics 2016 (Thesis reader, joint supervision with CH Schmid)
–Lisa Wang, MS in Biostatistics 2014 (Thesis reader, joint supervision with CH Schmid)
–Lauren Catalano, MD, Masters in Clinical and Translational Research Student (Thesis advisor)
–Alissa Trepman, MS, MPH Student (Thesis reader)

Undergraduate students
–Madeline Pesec, BS 2016 (Thesis reader)

Tufts University

Doctoral students

–Byron C. Wallace, PhD (Committee member)
–Winifred W. Yu, PhD (Committee member)

Tufts Medical Center

Masters students

–Kevin M. Small, PhD (for his CTS certificate)
–Georgios Kitsios, MD, MS
–Issa J. Dahabreh, MD, MS, (since, DSc)
–Annette Tobar, MD, MS
–Ezra Gabbay, MD, MS
–Christina Baik, MD, MS
–Laura Caprario, MD, MS
–Michael Kelly, MD, MPH, for his MS in CTS (Thesis committee member)

Other Mentees

I have mentored many students, fellows, or junior faculty in evidence-based medicine. I list the ones I have co-authored with:

–Alawi AlSheikh-Ali, MD, MS
–Daniel Kramer, MD
–Benjamin Wessler, MD
–Peter J. Castaldi, MD, MS
–Martin Wagner, MD
–Jose Calvo, MD
–Teruhiko Terasawa, MD, PhD
–Makiko Yoshida, PhD
–Denish Moorthy, MBBS
–Kamal Patel, MBA
–Jounghee Lee, PhD
–Haseeb Jafri, MD
–Angie May Rodday, MPH

–Yannis Koulouridis, MD

Mentor on career development awards (e.g., K grants)

K12	Institutional AHRQ-funded K12 in CER/PCOR at Brown University, Program Director TA Trikalinos
2013–2015	Agustin Yip, MD, PhD
	Lauren Catalano, MD
	Ijeoma Azodo, MD
2014–2016	Andrew Zullo, PharmD, PhD
	Francesca Beaudoin, MD, PhD
2016–2018	Yanick Brice, PhD
	Nishant Shah, MD, MS
2016–2019	Stacey Springs, PhD
2017–	Nina Joyce, PhD
2018–	Jonah Popp, PhD

K01	2016–: Valery Danilack, PhD, at Women and Infants Hospital. Primary Mentor.
K23	2016–: Ravi Bannuru, MD, PhD, at Tufts Medical Center. Mentor.
K23	2015–: David Barker, PhD, at Rhode Island Hospital. Mentor.
CoHSTAR	2015-2018: Daniel Pinto PT, PhD, at Northwestern University. Primary Mentor.